ABSTRACTS OF WORLD MEDICINE

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Pathology

496. **Schultz–Dale Test for Detection of Specific Antigen in Sera of Patients with Carcinoma**
P. BURROWS. *British Medical Journal* [*Brit. med. J.*] **1**, 368–370, Feb. 15, 1958. 8 refs.

With slight modifications, the method described by Makari (*Brit. med. J.*, 1955, **2**, 1291; *Abstr. Wld Med.*, 1956, **19**, 417), in which one of the most sensitive methods for detecting antigen, namely, measurement of the contraction of the guinea-pig uterine horns suspended in a Schultz–Dale bath, is used, has been applied by the present author at the Queen's University of Belfast in 207 cases of non-carcinomatous disease and 301 of histologically proved carcinoma. Of the latter, 291 (96·7%) gave a positive result, while of the control cases, 200 (96·7%) gave a negative result.

It is considered that the test is of some value in cases in which the possibility of carcinoma is raised in diagnosis. It has not been found to give any quantitative indication of the amount of tumour present in the body, since serum from a patient with a small carcinoma may produce as large a uterine contraction as serum from a patient with a large tumour. The test was found of most value in assessing patients who had had a carcinoma removed some time previously and had returned complaining of symptoms suggestive of recurrence of the original growth. In all such cases the test gave a positive result. Of the 7 false positive test results obtained in the non-carcinomatous group, 4 were in cases of nephrosis. The possible causes of this phenomenon are discussed. *L. A. Elson*

497. **Investigation of the Immunologically Active Constituent of Serum of Patients with Carcinoma**
D. BURROWS and D. W. NEILL. *British Medical Journal* [*Brit. med. J.*] **1**, 370–371, Feb. 15, 1958. 12 refs.

In investigations reported from the Queen's University of Belfast the authors attempted to identify the substance present in the serum of patients with carcinoma which is responsible for initiating the contraction of the immune guinea-pig uterus in the Schultz–Dale test described above [see Abstract 496]. Continuous paper electrophoresis was found to achieve reasonably good separation of the serum protein fractions without degradation. In all of 5 samples of serum from patients with carcinoma investigated by this method the immunologically active material appeared in collecting tubes immediately preceding the albumin fraction; this finding is thought to indicate that the substance is a protein or polypeptide of low molecular weight. It was not found in the serum of healthy subjects or of patients with non-carcinomatous diseases. It showed immunological features similar to those of carcinoma tissue, and is believed to be the active substance in the Schultz–Dale test for carcinoma.
L. A. Elson

498. **Electrophoretic Migration Pattern of Serum Glutamic Oxalacetic Transaminase**
H. G. SHEPHERD and H. J. MCDONALD. *Clinical Chemistry* [*Clin. Chem.*] **4**, 13–21, Feb., 1958. 3 figs., 18 refs.

Using an ultraviolet spectrophotometric technique the authors, working at Loyola University, Chicago, have assayed the glutamic oxalacetic transaminase (G.O.T.) activity of rat serum protein fractions, which were separated electrophoretically at *p*H 8·9. Maximal activity was found in the α_2-globulin region of the electrophoretic strip, although some activity, possibly a non-specific protein effect, was present in all the protein fractions. *M. Sandler*

499. **C-reactive Protein in Cancer: a Study of 216 Patients**
L. GRAF and M. M. RAPPORT. *Cancer* [*Cancer (Philad.)*] **11**, 255–258, March–April, 1958. 2 figs., 9 refs.

The sera of 216 patients with histologically proved cancer were tested for C-reactive protein by quantitative complement fixation. The results showed that a third of these did not have significant concentrations of CRP, and another third had very low concentrations (lowest tenth of the range). Many patients with metastases were without C-reactive protein.—[Authors' summary.]

500. **Vitamin B_{12} Excretion as Index of Hepatic Disorders. II. Correlation with Liver-function Tests**
H. BAKER, G. BRILL, I. PASHER, and H. SOBOTKA. *Clinical Chemistry* [*Clin. Chem.*] **4**, 27–31, Feb., 1958. 8 refs.

Hepatic disease has been shown to give rise to an increase in the vitamin-B_{12}-binding capacity of the serum. The authors have made use of this observation to demonstrate a correlation between certain of the empirical tests of liver function and the excretory response to the intramuscular administration of 60 μg. of vitamin B_{12}, the study being carried out on 38 patients at the Mount Sinai Hospital, New York, a majority of whom showed abnormal results in regard to serum total bilirubin and alkaline-phosphatase levels, albumin:globulin ratio, or the cephalin–cholesterol flocculation test. After the

intramuscular injection of 60 μg. of vitamin B_{12} the amount excreted in the urine during the following 8 hours was assayed microbiologically.

In 19 of the 22 patients with hepatic disorder there was decreased urinary excretion of vitamin B_{12}, that is, less than 10 μg. in 8 hours, whereas in the 16 patients without hepatic disease the urinary vitamin excretion was greater than 10 μg. in 8 hours. Low urinary excretion values were also noted in patients with rheumatic heart disease and lobar pneumonia. *M. Sandler*

HAEMATOLOGY

501. Alkaline Phosphatase in the White Cells in Leukaemia and Leukaemoid Reactions

B. J. LEONARD, M. C. G. ISRAËLS, and J. F. WILKINSON. *Lancet* [*Lancet*] **1**, 289–292, Feb. 8, 1958. 4 figs., 8 refs.

The authors, working at the Royal Infirmary and University of Manchester, describe a simple cytochemical technique for demonstrating alkaline phosphatase in leucocytes of the neutrophil series which is of value in distinguishing between myeloid leukaemia and leukaemoid reactions involving the myeloid series of cells. The method is as follows. The blood or marrow smears are fixed for 30 seconds in a mixture of 10 ml. formalin and 90 ml. absolute alcohol, washed, and incubated for 2 hours at 37° C. in freshly prepared buffer substrate solution containing 30 ml. of 10% sodium barbitone, 30 ml. of 3·2% sodium β-glycerophosphate, 30 ml. of M/10 magnesium sulphate, 45 ml. of 2% calcium nitrate, and 165 ml. of distilled water. The slides are then rinsed in distilled water containing a few drops of 2% calcium nitrate solution, immersed in 2% cobalt nitrate solution for 5 minutes, washed in a weak ammonium sulphide solution for 10 seconds followed by water, and counterstained with a 2% aqueous solution of safranine O for 10 seconds. As controls films of normal blood and of blood of known high leucocyte phosphatase activity are used. Alkaline-phosphatase activity is indicated by the presence of black granules in the cytoplasm of the neutrophil granulocytes, the result being expressed as absent, weak, or strong.

Normal leucocytes show weak activity (that is, only a few small black granules in the cytoplasm) or no activity. Cells giving a strongly positive reaction show many coarse black granules, or the whole cytoplasm may be black; such cells constitute less than 2% of the count in normal blood, but are plentiful in polycythaemia vera. In all of 50 cases of chronic myeloid leukaemia in all stages of the disease, irrespective of the leucocyte count or amount and type of treatment, alkaline-phosphatase activity was much reduced or absent. Investigation of 17 cases of myeloid leukaemoid reaction (associated with Hodgkin's disease in 6 cases, myelosclerosis in 3, and carcinomatosis, haemolytic anaemia, tuberculosis, and reticulosarcoma in 2 cases each) invariably showed a high proportion of strongly positive cells. In all these cases the cytological findings in the blood and bone marrow when examined by ordinary staining techniques were identical with those in myeloid leukaemia. The authors suggest that the determination of alkaline phosphatase in the leucocytes is at present the best, and often the only, method of distinguishing between chronic myeloid leukaemia and leukaemoid reaction involving the myeloid series of cells. They point out that the test is usually of no value in the diagnosis of acute leukaemia because blast cells contain no phosphatase. The precise role of alkaline phosphatase in the leucocytes is not known. *H. Caplan*

MORBID ANATOMY AND CYTOLOGY

502. Discrepancies in the Diagnosis of Genetic Sex by Leucocyte Morphology

D. J. B. ASHLEY and C. H. JONES. *Lancet* [*Lancet*] **1**, 240–242, Feb. 1, 1958. 3 figs., 19 refs.

In this paper from the David Lewis Northern and Alder Hey Children's Hospitals, Liverpool, the authors discuss discrepancies which were observed between the results of cytological diagnosis of genetic sex by different methods in 2 cases. Cytological techniques for the determination of sex are based on two differences in cellular morphology between the sexes. (1) In the normal female a characteristic mass of heterochromatin is seen lying adjacent to the nuclear membrane in a high proportion of the cells of the skin and other tissues, whereas this appearance is found in less than 10% of such cells in the normal male. (2) "Drumstick" satellites are found on the nuclei of more than 6 (1·2%) of every 500 mature polymorphonuclear leucocytes examined in the normal female and of less than 6 in the normal male. In the authors' cases examination of cells of the buccal mucosa showed heterochromatin to be present in less than 6% and in 4% of cells respectively, whereas on examination of blood films "drumsticks" were found on the nuclei of 3% and 7% of the leucocytes respectively.

During the past 2 years there have been many reports of discrepant results in the diagnosis of genetic sex by these two methods. These discrepancies, together with the cytological demonstration in leucocytes of typical sex-chromatin masses distinct from the nuclear satellites, indicate that "leucocyte morphology cannot be accepted as a valid criterion for the diagnosis of genetic sex". *E. Forrai*

503. Pathologic Changes in Adult Myxedema: Survey of 10 Necropsies

R. C. DOUGLASS and S. D. JACOBSON. *Journal of Clinical Endocrinology and Metabolism* [*J. clin. Endocr.*] **17**, 1354–1364, Nov., 1957. 4 figs., 29 refs.

In this paper from the Wayne County General Hospital, Eloise, Michigan, the authors describe the necropsy findings in 9 cases of primary adult myxoedema and one case of pituitary myxoedema. The histological features in the 9 primary cases were uniform. In the thyroid, such colloid as was present stained poorly. The residual follicles were atrophic, many appearing as aggregates of cells without a lumen. The epithelial cells had often undergone Hürthle-cell or squamous metaplasia, and

many were degenerative with pyknotic nuclei. Most of the parenchyma had been replaced by fibrous tissue, in which hyaline degeneration was common. Changes in other organs included atrophy of the cerebral cortex (5 cases), swelling and basophil degeneration of the myocardium, and marked distention of the colon (4 cases). There was widespread deposition of acid mucopolysaccharide and proliferation of mast cells in the connective tissues which, the authors suggest, may be related to the activity of the thyroid-stimulating hormone.

None of these features was observed in the case of pituitary myxoedema. *R. G. Rushworth*

504. **Post-mortem Observations on Contraction of the Human Ductus Arteriosus**

R. R. WILSON. *British Medical Journal* [*Brit. med. J.*] 1, 810–812, April 5, 1958. 1 fig., 8 refs.

It has been conclusively shown in experimental animals that active contraction of the ductus arteriosus is associated with the onset of respiration, and it is natural to assume that the same is true in man. Evidence supporting this assumption is presented in this paper, which reports the post-mortem findings in 100 newborn and stillborn infants examined at Paddington General Hospital, London. Of the 63 cases of neonatal death, the ductus was contracted in 46 and uncontracted in 11, whereas of the 37 cases of stillbirth, the ductus was contracted in 3 and uncontracted in 25 (being either partly contracted or dilated in the remainder in each group). Statistically, the correlation was highly significant ($\chi^2=37{\cdot}67$; $P<0{\cdot}001$). Further analysis of the findings reveals some rather interesting facts. Of the 63 newborn infants, 50 were premature, whereas 22 of the 37 stillborn infants were mature. There were more examples of uncontracted ductus among mature infants than among premature infants in both groups. Of the 46 cases of neonatal death with contracted ductus, 40 were premature and 18 weighed less than 1,250 g., whereas of the 11 with uncontracted ductus, 6 were mature. Of the 25 stillborn infants with uncontracted ductus, 16 were mature. These observations are the subject of speculation by the author, who [rightly] concludes that "the questions inherent in these findings require further study".

David Morris

505. **Study of the Air Content and State of Expansion of the Infant Lung.**

M. G. GOLDBERG and M. WOLMAN. *A.M.A. Archives of Pathology* [*A.M.A. Arch. Path.*] 65, 263–271, March, 1958. 14 figs., 18 refs.

A simple technique is described whereby inflation or deflation of individual lobes of the lung may be produced at necropsy and maintained during fixation. In an unselected series of 85 necropsies carried out at the Hadassah University Hospital, Jerusalem, on infants up to 2 years of age (including stillborn infants of at least 6 months' gestation), these procedures were carried out on two of the lobes and the histological appearances compared with those in the lobes not so treated, particular attention being paid to the appearance of the reticulin fibres. In lobes not artificially inflated or deflated areas of atelectasis were seen which were of three types: (1) a diffuse type associated with obstruction of larger bronchi or extensive uniform compression by overexpansion of adjoining areas; (2) polarized atelectasis with deformity of the alveoli, due to compression by adjoining overdistended parenchyma against the pleura or a fibrous septum; and (3) microatelectasis, seen mainly around overexpanded air vesicles. Similar changes were seen in artificially inflated lobes containing fluid, the unequal distribution of the injected air resulting in foci of atelectasis and foci of overexpansion.

The authors suggest the abandonment of the term "foetal atelectasis" and its replacement by "non-aeration". [The same suggestion has been already made by Morrison ("Foetal and Neonatal Pathology", London, 1952).] The term "dysaeration" is proposed to describe focal emphysema surrounded by micro-atelectasis. *H. S. Baar*

506. **The Microscopical Criteria of Interstitial Pneumonia**

M. WOLMAN and M. G. GOLDBERG. *A.M.A. Archives of Pathology* [*A.M.A. Arch. Path.*] 65, 272–278, March, 1958. 10 figs., 12 refs.

Every pathologist is familiar with the difficulty of differentiating between the appearances of "monocytic interstitial pneumonia" of the young infant and those of atelectasis. The present authors studied the microscopic characteristics of interstitial pneumonia as seen in the 85 infants whose investigation by special methods is described in the previous paper [see Abstract 505] and also in 11 cases of clear-cut interstitial pneumonia from which only paraffin sections were available. The appearances in sections stained by Laidlaw's silver impregnation method are described in detail. In interstitial pneumonia the reticulin fibres of the interalveolar septa are stretched and often form a thick band at the periphery of the septa on either side. Fragmentation of the reticulin fibres was frequently seen, there being a close association between this finding and pulmonary haemorrhage. Thickening of the interalveolar septa was very distinct in emphysematous inflated lungs.

H. S. Baar

507. **Squamous Metaplasia of the Respiratory Tract Epithelium. An Autopsy Study of 214 Cases. I. Incidence, Age and Sex Distribution.** [In English]

K. SANDERUD. *Acta pathologica et microbiologica Scandinavica* [*Acta path. microbiol. scand.*] 42, 247–264, 1958. 9 figs., 33 refs.

At the Grade Institute, University of Bergen, the author studied the incidence of squamous epithelial metaplasia in the lower trachea, main stem bronchi, and more distal branch bronchi at necropsy on 214 unselected subjects. No such changes were found in 15 stillborn or newborn infants, while among 12 infants of 1 to 11 months metaplasia was observed in one case only, that of a girl of 4 months dying of congenital heart defect and coarctation of the aorta. Among 11 children aged one to 9 years the incidence of squamoid change was 18% (2 cases), and among 7 aged 10 to 19 years it was 43% (3 cases), the

mean incidence in the 45 individuals under 20 years old being 13·3%. The mean incidence in the 169 adults was 59%. There was no clear correlation of incidence with age, but there was a marked sex difference, metaplastic changes being found in 70 of 100 men and only 30 (43·5%) of 69 women. One further marked difference became apparent when the sex incidence of single, double, and multiple metaplastic foci was determined, the figures for the males being 20, 17, and 33% and for the females 24·5, 13, and 5·5% respectively. *R. Salm*

508. **Myocardial Atrophy in Constrictive Pericarditis**
D. E. DINES, J. E. EDWARDS, and H. B. BURCHELL. *Proceedings of the Staff Meetings of the Mayo Clinic* [*Proc. Mayo Clin.*] **33**, 93–99, Feb. 19, 1958. 3 figs.

The authors investigated the occurrence of atrophy of the myocardium in constrictive pericarditis by measuring the thickness of the myocardial fibres in 14 cases and in 28 control cases at necropsy at the Mayo Clinic. Of the former group, 11 were cases of chronic constrictive pericarditis (mean duration 41 months), one was a case of fibrinous pericarditis of 4 weeks' duration, and 2 were cases of pericardial effusion of 10 and 15 months' duration respectively. The control group was made up of patients dying of causes other than cardiac or renal disease, 2 such patients being selected who were the same age and sex as each of the subjects in the first group. With an eyepiece micrometer 4 different readings of the diameter of the fibres were taken in each of 10 subepicardial, 10 mid-myocardial, and 10 subendocardial areas in the walls of both ventricles.

In each of the 11 cases of chronic constrictive pericarditis uniform myocardial atrophy, not confined to the areas underlying the adhesions, was found in both ventricles. The average difference in the thickness of the myocardial fibres between these cases and their control cases was 2·4 μ for the left ventricle and 2 μ for the right, the nuclei being more prominent in the former. There was no correlation between the degree of atrophy present and the duration of symptoms, the age of the patient, or the pericardial thickness. In the case of fibrinous pericarditis thinning of the fibres was confined to the area of the myocardium underlying the inflammatory process, but in the 2 cases of chronic pericardial effusion the atrophy was again generalized, the average difference in fibre thickness between these cases and their controls being 2·9 μ for the left and 2·8 μ for the right ventricle.
F. Hillman

509. **Gastric Mucosal Lesions Before and After Treatment in Iron Deficiency Anaemia**
F. LEES and F. D. ROSENTHAL. *Quarterly Journal of Medicine* [*Quart. J. Med.*] **27**, 19–26, Jan., 1958. 5 figs., 11 refs.

At the Royal Infirmary, Sheffield, the authors studied the changes in the gastric mucosa in 21 consecutive female patients (aged 28 to 65 years) with iron-deficiency anaemia without gastro-intestinal haemorrhage or ulceration. In 19 cases biopsy specimens of gastric mucosa were obtained before treatment and one year after correction of the anaemia; in the remaining 2 cases a second specimen was not available. Only 2 of the 19 first specimens were normal; the remainder showed inflammatory infiltration of the substantia propria of varying severity. Atrophy was present in 11 of the specimens. No relationship was found between the degree of anaemia and the severity of the lesion. Examination of the specimens after treatment showed that the gastric mucosal lesions of infiltration and atrophy had not improved and in some instances had actually progressed although the anaemia was corrected. The results of acid secretion tests also failed to reveal any improvement.

It is concluded that the gastric lesions precede the anaemia, and that they are in some way concerned in the aetiology of iron deficiency. *A. W. H. Foxell*

510. **Kidney Biopsy in Acute Glomerulonephritis.** [In English]
C. BRUN, H. GORMSEN, T. HILDEN, P. IVERSEN, and F. RAASCHOU. *Acta medica Scandinavica* [*Acta med. scand.*] **160**, 155–163, March 7, 1958. 6 figs., 4 refs.

At the Kommunehospital, Copenhagen, renal needle aspiration biopsy was performed 15 times in 13 cases of clinically diagnosed acute glomerulonephritis at varying stages of the disease. The results were correlated with the natural course of the disease, as judged by clinical appraisal, 24-hour endogenous creatinine clearance, and the results of routine laboratory tests for blood and urine constituents. Of 7 patients with severe disease, all of whom were uraemic and had low creatinine clearance (less than 3 ml. per minute), all died, the longest survival being 10 months from the first appearance of symptoms. In these cases the structural changes in the kidneys were marked, the glomeruli being uniformly the seat of fibrinoid necrosis, with endothelial and epithelial proliferation, crescent formation, and interstitial inflammation. The 6 patients who recovered showed, during the acute phase, creatinine clearance values ranging from 46 to 116 ml. per minute and mild to moderate changes in the renal structure, there being some glomerular hyalinization and endothelial and epithelial proliferation, but no fibrinoid necrosis or crescent formation

The considerable difference in the severity of the pathological changes between the two groups is commented upon, and the authors suggest that the possibility that there may be two fundamentally different types of acute glomerulonephritis cannot be excluded. The cases in this series were all of Ellis's Type-I nephritis (*Lancet*, 1942, **1**, 1, 34, and 72), the severe cases corresponding to Ellis's cases with rapidly progressive course, and the mild cases to those with subsequent recovery or slow progression. Histologically, there was a discrepancy between the structural dating of the lesions and the " clinical age " of the disease. This is explained on the grounds that either these cases were in fact a recrudescence of earlier acute disease of subclinical intensity, or that histological dating may give erroneous results, based as it has been so far on post-mortem material. The authors consider that further biopsy studies may lead to a revision of our present concepts of the histological changes in acute glomerulonephritis. *J. B. Cavanagh*

Microbiology and Parasitology

511. **Isolation of Cytopathogenic Agents from the Respiratory Tract in Acute Laryngotracheobronchitis**
A. J. Beale, D. L. McLeod, W. Stackiw, and A. J. Rhodes. *British Medical Journal* [*Brit. med. J.*] **1**, 302–303, Feb. 8, 1958. 4 figs., 13 refs.

At the Hospital for Sick Children, Toronto, detailed virus studies were carried out on 15 infants with acute laryngotracheobronchitis (croup), nasopharyngeal or tracheal secretions being inoculated into tissue culture systems which included both HeLa and human amnion cells. From 10 of the patients cytopathogenic agents were isolated, more frequently from tracheal than nasopharyngeal specimens and also more commonly in amnion-cell than in HeLa-cell cultures. Human amnion cells were considered to be superior because of the greater ease of maintenance of healthy cultures. The viral agents were slow, however, to produce cytopathogenic effects, requiring 17 or more days on primary isolation. These effects were distinctive; in amnion-cell cultures the changes resembled a sponge or Gruyère cheese, whereas in HeLa-cell systems clumping of the cells with loss of cell walls to give multinucleated giant cells occurred. These changes are unlike those produced by adenoviruses or poliomyelitis, Coxsackie, and E.C.H.O. viruses, but are similar to those described as being produced by measles virus, although no intranuclear inclusions were observed. One virus strain agglutinated chick and to a lesser extent human erythrocytes at 4° C., indicating some resemblance to the influenza–mumps–N.D.V. group of viruses. In 6 of the patients specific neutralizing antibodies were demonstrated in the convalescent serum, suggesting that these agents were causally related to the upper respiratory tract infection studied.

D. Geraint James

512. **Personal Experience of New Microbiological Methods in the Diagnosis of Typhoid and Paratyphoid Fevers.** (Unsere Erfahrungen mit neuen mikrobiologischen Untersuchungsmethoden in der Diagnostik von Typhus-Paratyphuserkrankungen)
J. Havlík and J. Švejcar. *Zentralblatt für Bakteriologie, Parasitenkunde, Infektionskrankheiten und Hygiene. I. Abt. Orig.* [*Zbl. Bakt., I. Abt. Orig.*] **170**, 438–452, 1958. 5 figs., 24 refs.

From the Faculty of Hygiene, Prague, the authors describe a technique for the rapid isolation of *Salmonella* organisms from blood by membrane filtration. Blood, haemolysed by incubation at 37° C. with 1% trypsin solution, is filtered through a membrane of a mean pore diameter of 300 mμ, which is then placed on the surface of a plate containing a suitable medium, such as that of Wilson and Blair. Typical, though small, *Salmonella* colonies appear after 18 to 48 hours' incubation. With blood from rabbits experimentally infected with *Salm. typhosa* the membrane-filtration technique and conventional blood culture gave identical results, while in cases of *Salmonella* infection in man positive results were obtained rather more frequently with the former technique than the latter. The authors' technique was also found to give satisfactory results with sternal marrow and (omitting the treatment with trypsin) also with bile and urine.

The isolation of *Salmonella* organisms from faeces may be conveniently carried out by means of a rectal tampon consisting of cotton wool dipped in melted deoxycholate agar. A scheme is given for the isolation and identification of *Salmonella* from the stools in 3 days.

M. Lubran

513. **Anaerobes in Routine Diagnostic Cultures**
E. J. Stokes. *Lancet* [*Lancet*] **1**, 668–670, March 29, 1958. 5 refs.

Over a recent 6-year period at University College Hospital, London, over 5,000 specimens were cultured, both aerobically and anaerobically, to assess the incidence of anaerobes in routine diagnostic cultures. Specimens of faeces and skin and those from the vagina, upper respiratory tract, and chronically discharging ears were excluded.

Aerobic cultures were made on horse-blood agar plates and then incubated in air with the addition of 5 to 10% carbon dioxide, and anaerobic cultures in the presence of 2% CO_2. The CO_2 was found to improve growth in some instances. Of 5,394 specimens, 4,737 showed growth. Of these, 496 yielded anaerobes, and in 139 the anaerobes were in pure culture. Anaerobic organisms were recovered from all types of specimen, particularly specimens from abdominal abscesses, Bartholin's abscesses, ischiorectal abscesses, and infected sebaceous cysts, and also specimens of fluid from cases of peritonitis and pleurisy.

The author points out that cultures should not be reported as sterile if anaerobic culture has not been attempted. If anaerobic culture cannot be carried out on receipt of the specimen the swab should be left in a transport medium until a more convenient time.

E. G. Rees

514. **Antibody Response in Volunteers to Asian Influenza Vaccine**
M. R. Hilleman, F. J. Flatley, S. A. Anderson, M. L. Luecking, and D. J. Levinson. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **166**, 1134–1140, March 8, 1958. 1 fig., 10 refs.

At the Walter Reed Army Institute of Research, Washington, D.C., the authors studied the antibody response of 619 persons who were given Asian or polyvalent influenza vaccine in varying doses by various routes during the period July to September, 1957, before their exposure to epidemic Asian influenza. Three lots,

differing in strength, of monovalent Asian influenza vaccine prepared from Strain A/Japan/305/57 and a combined polyvalent (A, A′, and B) vaccine without the Asian strain were used. The injections were given subcutaneously or intradermally on two occasions at 3 weeks' interval, the subjects' blood being tested for haemagglutination inhibiting antibody before and after vaccination.

Although the titre of the antibody response was dependent upon the dosage, the majority of subjects showed some response to Asian vaccine even in doses as small as 62·5 chick cell agglutinating (C.C.A.) units, while the response to two doses of 250 C.C.A. units was as great as that seen in proved clinical cases of the disease. (Precise information concerning the serum level of haemagglutination inhibiting antibody required for protection against Asian influenza is at present lacking.) Mild reactions occurred in 18 out of 91 persons who received 1,000 C.C.A. units of Asian vaccine, characterized by local soreness at the site of the injection, a rise of temperature up to 102° F. (38·9° C.), and mild malaise.

The injection of polyvalent influenza vaccine did not induce the formation of antibodies against the Asian virus, nor did it enhance the antibody response to the subsequent injection of Asian vaccine. Immunization with Asian vaccine, however, stimulated a small antibody response against Type A/Swine/30 and Type A′/Hawaii/303/56 viruses. The response to the intradermal injection of 0·1 ml. of Asian vaccine was the same as that to 1 ml. given subcutaneously. *Franz Heimann*

515. **Serological Responses in Infantile Gastro-enteritis**
W. McNAUGHT. *Journal of Pathology and Bacteriology* [*J. Path. Bact.*] **75**, 307–312, 1958. 10 refs.

Tests were carried out at Ruchill Hospital, Glasgow, on specimens of serum from cases of infantile gastro-enteritis for the presence of antibodies to the homologous faecal strains of *Escherichia coli*. Agglutinins have been found to be demonstrable in the serum in such cases only irregularly and in low titres by direct bacterial agglutination tests. However, Neter *et al.* (*J. exp. Med.*, 1952, **96**, 1) have claimed that haemagglutination of sensitized erythrocytes is a more sensitive method of demonstrating serum antibodies to coliform organisms, and both methods were therefore used on each serum sample tested in the present investigation. The haemagglutination test consists in adsorbing bacterial antigens on to the surface of washed human or other erythrocytes and challenging the cells thus sensitized with the serum to be tested, macroscopic agglutination of the erythrocytes indicating the presence in the serum of agglutinins to the sensitizing bacteria. In a preliminary trial haemagglutination tests for bacterial O agglutinins were carried out in parallel with conventional bacterial O-agglutination tests; 32 different strains of *Esch. coli* of four serological types were used and tested against rabbit antisera prepared to these four types, the results showing the two tests to be of much the same sensitivity.

In the clinical investigation 58 babies with gastro-enteritis admitted consecutively were studied. A stool or rectal swab from each was tested for *Esch. coli* types on admission, OB antisera to *Esch. coli* O Groups 111, 55, 26, 86, 125, 126, 127, and 128 being used for typing. When a typable strain was isolated, or when cross-infection with a typable strain subsequently occurred, one representative colony was subcultured for use in agglutination tests with that patient's serum. Specimens of venous blood were taken for serological testing from each patient on admission and again 10 to 20 days later. Specific types of *Esch. coli* were isolated from the faeces on admission in 17 of the 58 cases, while 28 patients became cross-infected with a specific type while in hospital. Agglutinins to the homologous faecal strain of *Esch. coli* were demonstrated in the serum in 9 cases only, and only 3 of these were harbouring strains known to be associated with gastro-enteritis. Where antibody response was present the titres obtained were generally of a low order and involved O antibodies only. The titres obtained with the two tests were closely similar, and the author concludes that " on this basis, haemagglutination has not been shown to be more sensitive than standard bacterial agglutination for the demonstration of serum O-agglutinins in infants ". No correlation was found between the serological findings and clinical severity, as judged from the presence or absence of diarrhoea and dehydration, and " no evidence for the pathogenicity of specific types of [*Esch.*] *coli* was demonstrable by serological tests on babies harbouring these organisms ".
I. Berkinshaw-Smith

516. **On the Nature of the Mitsuda and the Kveim Reaction.** [In English]
R. KOOIJ and T. GERRITSEN. *Dermatologica* [*Dermatologica* (*Basel*)] **116**, 1–27, Jan., 1958. 6 figs., bibliography.

The histological background of the Mitsuda, Fernandez, and Kveim tests is discussed, and the results of investigations carried out on patients with leprosy at the Westfort Institution, Pretoria, are presented. Positive Mitsuda reactions were obtained with suspensions of normal liver particles in patients with tuberculoid (but not with lepromatous) leprosy, the reactions being similar to those obtained with lepromin containing leprosy bacilli. Negative Mitsuda reactions are obtained with filtrates of suspensions of normal liver or lepromin suspensions, and it is concluded that particulate matter is essential for the reaction, which is considered to be " a sarcoid (tuberculoid) type of foreign body reaction or an isomorphic phenomenon ". In patients with tuberculoid leprosy minute papules were observed at the site of intradermal injection of Kveim antigens, consisting of suspensions of various tissues from patients with sarcoidosis. Biopsy of some of the papules is reported to have shown a tuberculoid structure. The Kveim reaction is considered to be " an expression of a sarcoid mode of reaction in certain individuals ".

[From the context it seems possible that the authors attribute the same significance to a tuberculoid histology as they do to a non-specific, foreign-body, giant-cell reaction. If so, this would profoundly influence the interpretation of their results, conclusions, and deductions.] *D. Geraint James*

Pharmacology and Therapeutics

517. **Effect of Chlorothiazide on the Hypotensive Action of Mecamylamine and on Its Urinary Excretion**
M. HARINGTON and P. KINCAID-SMITH. *Lancet* [*Lancet*] 1, 403–404, Feb. 22, 1958. 2 figs., 7 refs.

It has been reported that chlorothiazide potentiates the action of many hypotensive drugs, including mecamylamine. At the Postgraduate Medical School of London the authors studied the effect of chlorothiazide on the urinary excretion of mecamylamine in 3 patients under treatment with the latter drug. Administration of 0·5 g. of chlorothiazide 3 times a day was followed by a significant reduction in the daily urinary excretion of mecamylamine. When chlorothiazide only was given to 4 further patients in a single dose of 0·5 g. intravenously no fall in blood pressure was observed, although there was a pronounced sodium diuresis. The authors consider it unlikely that chlorothiazide has any direct hypotensive action of its own. In their view its potentiating effect on mecamylamine is due, in part, to the retention of the latter in the body which it brings about.

Bernard Isaacs

518. **Nitroglycerin and Other Nitrites in the Treatment of Angina Pectoris**
J. E. F. RISEMAN, G. E. ALTMAN, and S. KORETSKY. *Circulation* [*Circulation*] **17**, 22–39, Jan., 1958. 2 figs., bibliography.

Nitroglycerin is the most commonly used drug for preventing attacks of angina pectoris, its one drawback being its short duration of action. At the Beth Israel Hospital (Harvard and Tufts Medical Schools), Boston, a comparative trial of nitroglycerin and 5 other nitrites was carried out on 34 patients with angina pectoris due to coronary arterial disease in the hope of finding an equally effective but longer acting drug. The patients were first observed for many weeks to evaluate the severity and constancy of their symptoms, an exercise tolerance test being performed under standardized conditions once a week. The various nitrites and placebos in various forms, colours, and concentrations were then administered in turn by the double-blind technique. Each was given for at least a week before an exercise tolerance test was performed to assess its effect, a dose of the drug being given immediately before the test. Observations were also made of the clinical response and of changes in the exercise electrocardiogram (ECG). The drugs were given sublingually, orally (swallowed), by subcutaneous or intramuscular injection, and by inunction. A beneficial effect was invariably checked by administration of a placebo followed later by the same drug in a different form, though neither the patient nor the observer who administered the exercise tolerance test was aware of this procedure. The preparations used, the chemical and physical characteristics of which are briefly described, were: (*a*) nitroglycerin; (*b*) erythrol tetranitrate; (*c*) mannitol hexanitrate; (*d*) triethanolamine trinitrate biphosphate; (*e*) pentaerythritol tetranitrate; and (*f*) sodium nitrate. The dose in each case was initially that recommended by the manufacturer, but was increased if this proved inadequate.

Drugs (*a*), (*b*), (*c*), and (*d*) were all much more effective when taken sublingually than when swallowed. Drugs (*a*) and (*b*) were the two most effective prophylactic agents, while the long duration of action of the latter (1 to 2 hours) made it especially valuable for clinical use. These drugs were also effective when given parenterally and percutaneously, but were inactivated when swallowed. Drugs (*c*) and (*d*) were effective sublingually, but the latter frequently caused glossitis. Drugs (*e*) and (*f*) were found to be of limited value. Depression of the S–T segment in the ECG after exercise was diminished appreciably in 6 out of 7 subjects receiving Drug (*a*) sublingually and in all of 4 receiving Drug (*b*) sublingually. Headache occurred in some cases after taking Drug (*b*); it could be avoided by decreasing the dose of the drug or relieved with aspirin. Hypotensive reactions occurred in more than one-third of the patients receiving Drug (*f*).

D. Goldman

519. **Dichlorphenamide as a Diuretic Agent**
J. B. ROCHELLE, J. H. MOYER, and R. V. FORD. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **235**, 168–178, Feb., 1958. 8 figs., 1 ref.

A laboratory and clinical study of the diuretic properties of dichlorphenamide (" daranide ") is reported from Baylor University College of Medicine and the Veterans Administration Hospital, Houston, Texas.

In the experimental investigation dogs, which were not hydrated, were anaesthetized and, after a control period of one hour during which urine was collected, were given dichlorphenamide, 0·5 to 10 mg. per kg., by intravenous injection. There was a significant increase in urine volume within 30 minutes of the injection, the period of diuresis varying from 1½ to over 4 hours according to dosage. There was also an increase in sodium and, to a lesser extent, potassium excretion.

The clinical observations were made on 20 ambulatory patients with controlled heart failure. These were kept in a metabolic ward and their intake of water and sodium was rigorously controlled. Oral administration of 2 doses of 50 mg. dichlorphenamide in the 24 hours caused a slight increase in excretion of sodium, potassium, and bicarbonate and, to a lesser extent, of chloride; urinary *p*H remained raised. A single dose of 500 mg. of the drug produced changes which lasted for 6 hours only; there was a rather lower excretion of potassium and bicarbonate and a higher excretion of chloride than with smaller doses. Optimal dosage was 50 to 100 mg. given as a single dose; amounts over 200 mg. produced anorexia, nausea, and vomiting, with dizziness, ataxia, tremor, and tinnitus. After oral administration of 100 mg. of dichlorphenamide an increase in sodium excretion

occurred comparable with that following 1 ml. (40 mg.) of meralluride given intramuscularly.

It is concluded that dichlorphenamide is a diuretic of moderate potency, useful especially in the treatment of mild cardiac failure or, where the failure is more severe, for prolonging the period between injections of mercurial diuretics. It is suitable for continuous administration, as it is not so liable to cause acidosis as other carbonic anhydrase inhibitors.

W. H. Horner Andrews

520. **Clinical and Laboratory Observations on Two Trifluoromethyl Phenothiazine Derivatives**
J. H. MOYER and P. K. CONNER. *Journal of Laboratory and Clinical Medicine* [*J. Lab. clin. Med.*] **51**, 185–197, Feb., 1958. 4 figs., 4 refs.

The usefulness of chlorpromazine as an antiemetic drug is limited by the fact that not all types of nausea and vomiting respond well to it, while side-reactions are often troublesome. This paper from Baylor University College of Medicine, Houston, Texas, reports the results of laboratory and clinical trials of two new antiemetic agents related chemically to, but more potent than, chlorpromazine. The substances studied were SKF 4648 (10 - (3′ - dimethylaminopropyl) - 2 - trifluoromethyl - phenothiazine hydrochloride) and SKF 5019 (10-(3′-(1″-methylpiperazinyl - 4″) - propyl) - 2 - trifluoromethyl-phenothiazine dihydrochloride).

On comparison of the effects of the two new drugs and chlorpromazine on apomorphine-induced vomiting in 10 dogs SKF 4648 was found to be the most potent antiemetic, a dose of 0·2 mg. per kg. body weight given intravenously consistently inhibiting vomiting when threshold doses of apomorphine were used. In the same dosage SKF 5019 inhibited vomiting in 4 of 5 dogs and chlorpromazine in only 4 of 10 dogs. Neither of the new drugs was effective against vomiting induced by the oral administration of copper sulphate. The antiemetic properties of the three compounds were also compared in 29 in-patients complaining of nausea or vomiting. It was found that SKF 4648 was more potent than chlorpromazine and that its action lasted longer (8 to 10 hours). The effectiveness of SKF 5019 appeared to be equal to that of chlorpromazine.

Laboratory tests on dogs for possible side-effects showed that neither of the new compounds affected water or electrolyte excretion significantly or consistently during the 3 hours after their intravenous injection. No significant effect on renal haemodynamics was noted with either drug. SKF 4648 was found to be more liable to cause a fall of blood pressure than SKF 5019. Both drugs consistently deepened the anaesthesia produced by pentobarbitone. The response to noradrenaline was reduced by SKF 4648 in doses of 1 mg. per kg., though never by more than 50%, whereas SKF 5019 produced only minimal adrenergic block in the same dosage. A clinical study of the acute toxic effects of the drugs was made on 5 normal subjects, who each received both drugs intramuscularly, and on 28 in-patients (16 of whom had nausea or vomiting, the other 12 acting as controls), who were given one or other drug by mouth. The chief findings in this [very limited] trial were that SKF 5019 seemed to have a greater soporific effect and to be more liable to produce psychic changes than SKF 4648. The acute toxic reactions noted included weakness, apprehension, dizziness, blurring of vision, and altered emotional response. The chronic toxic effects were studied in 29 in-patients and 50 out-patients, the drugs being given for varying periods up to 8 weeks. Liver function tests, examination of the blood and urine, and electrocardiography were carried out weekly and revealed no abnormality apart from a slight and usually transient rise in the thymol turbidity level in 8 of the out-patients. The most troublesome chronic toxic effects were the psychic changes, especially agitation, anxiety, and insomnia. These effects were not produced when the drug was replaced by a placebo. The authors suggest that "these so-called side effects may become valuable assets when the agents are used to treat psychiatric illness". They finally conclude that "SKF 4648 is a potent antiemetic, which is more effective than chlorpromazine. However, because of the side effects it should be reserved for patients with severe nausea and vomiting who do not respond to antiemetic agents which have less severe side effects".

I. Berkinshaw-Smith

521. **A Potent Central Analgesic, "R 875" (D-2:2-Diphenyl-3-methyl-4-morpholinobutyrylpyrrolidine). Its Applications in Neurology.** (Un analgésique central puissant: le R 875. Le 2:2-dyphényl-3-méthyl-4-morpholino-butyryl-pyrrolidine base dextrogyre. Son application en neurologie)
G. BOUDIN and J. BARBIZET. *Presse médicale* [*Presse méd.*] **66**, 131–134, Jan. 25, 1958. 5 refs.

Pharmacological studies have shown D-2:2-diphenyl-3-methyl-4-morpholinobutyrylpyrrolidine base ("R 875") to be the most potent analgesic known. Experimentally, it was shown in cats and dogs to be 10 times as potent as morphine and of low toxicity. The present paper from the Hôpital Saint-Antoine, Paris, is concerned with its use in painful neurological conditions. In many of these, including subarachnoid haemorrhage, tuberculous meningitis, post-ventriculography headache, and root pain due to pressure of secondary malignant deposits, the results have been satisfactory. In addition, in such notoriously intractable conditions as the thalamic syndrome, trigeminal and atypical neuralgia, postherpetic neuralgia, and tabetic lancinating pains a good response was obtained in the majority of cases. All of 4 patients with painful amputation stumps obtained relief on administration of the drug. On psychogenic pain, however, R 875 was without effect, in spite of an objective raising of the pain threshold.

Serious side-effects such as nystagmus and depression of respiration occurred only after intravenous administration. This route, however, is usually unnecessary, as the drug is effective by mouth or by subcutaneous injection, and then produces only minor symptoms such as pallor, malaise, nausea, and vomiting. In no case was the patient's intellect affected. The authors have now treated more than 100 patients over a period of 8 months and so far there has been no evidence of either tolerance or habituation to the drug. *R. Schneider.*

Chemotherapy

522. **Antibiotic Combinations. Antibacterial Action of Plasma after Ingestion of Novobiocin or Penicillin G or Both**

W. F. JONES and M. FINLAND. *New England Journal of Medicine* [*New Engl. J. Med.*] **257**, 1268–1274, Dec. 26, 1957. 5 figs., 22 refs.

This paper from the Thorndike Memorial Laboratory (Harvard Medical School), Boston City Hospital, reports observations on the antibacterial action of the plasma of healthy subjects following the ingestion of novobiocin and benzylpenicillin, singly or in combination. Four organisms, *Streptococcus* 98, *Staphylococcus* 209 P and 400, and *Sarcina lutea*, were tested against serial dilutions of the test plasma in broth, and control tests were made with solutions of the antibiotics in broth containing final concentrations of 6·25 and 50% of plasma, this being to allow for the known binding of novobiocin by plasma.

No evidence was found of a synergistic action of novobiocin with penicillin, and in fact with *Staphylococcus* 400, which is an organism highly resistant to penicillin, there was a suggestion that the presence of penicillin might antagonize the activity of novobiocin. It was also shown that in the presence of 50% plasma 95% of the activity of novobiocin was inhibited. *E. G. Rees*

523. **Dermatitis Caused by Penicillin in Milk**

H. R. VICKERS, L. BAGRATUNI, and S. ALEXANDER. *Lancet* [*Lancet*] **1**, 351–352, Feb. 15, 1958. 19 refs.

Two cases of dermatitis have been seen at the Radcliffe Infirmary, Oxford, in which the allergen was considered to be the penicillin present in cows' milk. One patient had previously suffered from penicillin dermatitis and the other was known to have drunk milk from a penicillin-treated cow. One sample of milk contained 4 units per ml. Attention is drawn to the clinical risks arising from the now common use of penicillin in the treatment of bovine streptococcal mastitis. It is suggested that no milk from such animals should be sold until 72 hours after the last injection, when the chance of its containing penicillin will be less and the risk of allergic reactions reduced. *Kenneth Gurling*

524. **Sulfamethoxypyridazine: a New Sulfonamide for Pediatric Outpatients**

C. WEIHL. *Antibiotic Medicine and Clinical Therapy* [*Antibiot. Med.*] **5**, 173–181, March, 1958. 3 refs.

After a brief review of the history of sulphonamide drugs and a description of the chemistry and pharmacology of sulphamethoxypyridazine the author reports, from the University of Cincinnati College of Medicine, Ohio, a trial of sulphamethoxypyridazine in 105 outpatients at a paediatric clinic. These varied in age from 6 weeks to 15 years, 52·3% being under the age of one year and 8·6% older than 5 years. Most of the patients (102) had respiratory infections; 2 had gastro-enteritis and one cystitis. The preparations used were a syrup containing 50 mg. of the drug per ml. and tablets of 0·5 g. each. Doses were between 30 and 40 mg. per kg. body weight on the first day and between 15 and 20 mg. per kg. subsequently for 6 days. No special attempt was made to increase water intake.

Clinical improvement within 24 hours of starting treatment was classified as an " excellent " response, and improvement occurring within 48 hours as " satisfactory ". There were 41 cases in the " excellent " and 46 in the " satisfactory " groups—a total of 87 cases. Cases in which there was no clinical response within 72 hours were labelled " unsatisfactory "; these numbered 14. In 4 cases the illness was progressive or a relapse took place.

Random samples of blood were taken between the 4th and 7th days of treatment and at intervals of 4 to 24 hours after the most recent dose of drug, and the sulphonamide content was estimated. The median level was 6·0 mg. per 100 ml., with a range from 0·75 to 15·5 mg. per 100 ml.; 63·8% of the estimations were within the range 4·0 to 10·0 mg. per 100 ml.

Only 4 children presented any problems in the administration of the drug. There were no instances of granulocytopenia, crystalluria, albuminuria, or haematuria. In 2 cases drug fever developed, on the 5th and 6th days of treatment respectively; one child developed urticaria on the 7th day and one a morbilliform rash on the 3rd day. All these untoward reactions cleared within 72 hours of the cessation of therapy. A 3-year-old child who accidentally took 900 mg. of the drug 2 weeks after the end of treatment developed fever within 48 hours and a rash which lasted 6 days. Two patients developed staphylococcal infections while under treatment.

In discussing his findings the author emphasizes the ease of administration of sulphamethoxypyridazine, the satisfactorily low incidence of side-effects, and the ability to maintain therapeutic blood levels in children with a single daily dose of only 15 mg. per kg. body weight.

Charles Rolland

525. **The Effect of Thiocarbanidin and Related Compounds on *Mycobacterium tuberculosis* var. *hominis in vitro* and *in vivo***

G. P. YOUMANS, A. S. YOUMANS, and L. DOUB. *American Review of Tuberculosis and Pulmonary Diseases* [*Amer. Rev. Tuberc.*] **77**, 301–310, Feb., 1958. 12 refs.

The authors have investigated the tuberculostatic activity of a large number of thioureas, and in the present paper describe an evaluation of 24 representative compounds, consisting of 7 phenylalkylthioureas and 17 thiocarbanilides. For the tests *in vitro* drug dilutions were made in tubes of modified Proskauer and Beck medium, which were then inoculated with a standard amount of the H37Rv strain of *Mycobacterium tuberculosis* and incubated for 14 days. Mice were used for

the animal experiments, the drug being incorporated in the diet for 14 days following the intravenous injection of tubercle bacilli.

The 7 phenylalkylthioureas were shown to have only low activity both *in vitro* and *in vivo*. The 17 thiocarbanilides showed much greater activity *in vitro*, but this was reduced to a low order on the addition of serum to the medium. The activity of the thiocarbanilides *in vivo* was comparable, even in low doses, to that of PAS, and this activity did not increase with the size of the dose. It is suggested that thiocarbanidin, the most promising of the thiocarbanilides, might prove useful as a substitute for PAS with streptomycin or isoniazid in the treatment of tuberculosis. *E. G. Rees*

CHEMOTHERAPY OF TUMOURS

526. **Investigation of the Relation between Clinical and Tissue-culture Response to Chemotherapeutic Agents on Human Cancer**

J. C. WRIGHT, J. P. COBB, S. L. GUMPORT, F. M. GOLOMB, and D. SAFADI. *New England Journal of Medicine* [*New Engl. J. Med.*] **257**, 1207–1211, Dec. 19, 1957. 2 figs., 7 refs.

In a comparative study carried out *in vivo* and *in vitro* at New York University Post-Graduate Medical School portions of tumour biopsy tissue from 40 proven cases of cancer grown in tissue culture were treated with the same chemotherapeutic agent as was the patient from whom the specimen was taken. In 26 cases there was good correlation between the clinical response of the patient and the result in tissue culture; in 10 cases there was no apparent correlation and in 4 the results were equivocal. It is suggested that the technique might provide a useful screening method in the choice of the best chemotherapeutic agent for use in the treatment of neoplastic disease. *G. Calcutt*

527. **Preliminary Results of Treatment of Malignant Tumours with a New Mustine Derivative.** (Erste Erfahrungen in der Behandlung maligner Tumoren mit einem neuen N-Lost-Phosphamidester)

R. GROSS and K. LAMBERS. *Deutsche medizinische Wochenschrift* [*Dtsch. med. Wschr.*] **83**, 458–462, March 21, 1958. 2 figs., 4 refs.

" Endoxan " (N:N-bis-(β-chlorethyl)-N′:O-propylene-phosphoric acid ester diamide) is a new compound related to nitrogen mustard (mustine) which, in animals, shows good cytostatic activity against tumours combined with low toxicity (Brock and Wilmanns, *Dtsch. med. Wschr.*, 1958, **83**, 453). At the Medical Clinic of the University of Marburg 62 patients with malignant growths have been treated with this drug. It was given initially by the intravenous route, the dose being 150 mg. daily or 100 mg. twice daily, though a few patients had more than this. The total intravenous dosage was generally between 2 and 7 g., but as much as 10 g. was given in one case. Maintenance therapy was then continued by mouth, 80 to 100 mg. being given daily to a total dose of as much as 25 g.

Side-effects, consisting in anorexia, nausea, and vomiting, appeared in some cases with a daily intravenous dose of 200 mg., and in nearly all when a larger dose was tried. Oral treatment did not cause side-effects in the dosages used. Toxic effects on the bone marrow were seen in 7 cases, in 6 of which there was mild to moderate leucopenia, lymphocytes and granulocytes being equally affected, and in one there was a moderate thrombocytopenia. All 7 patients had had more than 5 g. of the drug, and in all the blood changes were readily reversible. Two other patients developed alopecia.

The results were classed as " very good " in 4 out of 5 patients with lymphosarcoma, all of whom showed marked regression of the tumour masses with prolonged remission on cessation of treatment on at least one occasion; in the fifth patient the result was " good ". Some benefit was observed in 3 out of 4 patients with Hodgkin's disease and in a few patients with chronic myeloid leukaemia. In most patients with chronic myeloid leukaemia and in the great majority of patients with carcinoma the results were disappointing, though one patient with distant metastases from a bronchial carcinoma showed great improvement under treatment. One patient with lymphosarcoma, who relapsed after a successful first course of the drug, responded equally well to a second course. *P. Mestitz*

528. **Studies on the Carcinostatic Activity in Mice of 6-Azauracil Riboside (Azauridine), in Comparison with That of 6-Azauracil**

J. J. JAFFE, R. E. HANDSCHUMACHER, and A. D. WELCH. *Yale Journal of Biology and Medicine* [*Yale J. Biol. Med.*] **30**, 168–175, Dec., 1957 [received Feb., 1958]. 21 refs.

6-Azauracil and its riboside, azauridine, have been tested at Yale University School of Medicine for carcinostatic activity against lymphomata L1210 and L5178Y and sarcoma 180 in mice. By intraperitoneal injection or by mouth azauridine was 10 to 20 times more effective than its parent base and showed little toxicity. *G. Calcutt*

529. **Triethylenephosphoramide in the Treatment of Disseminated Melanoma**

J. L. TULLIS. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **166**, 37–41, Jan. 4, 1948. 5 refs.

The effects of administering triethylene-phosphoramide (TEPA) and a related sulfur compound (thio-TEPA) were studied in 13 out of 15 patients treated for malignant melanomas. Given either intravenously or orally in doses just sufficient to decrease either the leukocyte or the platelet count, these drugs in one case caused striking changes in pigment metabolism. These changes included the blanching of existent skin blemishes and the decoloration of eyebrows, facial hair, and skin generally. Inhibition of the bone marrow by these doses proved to be temporary. The treatment did not save patients near death, but in two well-advanced cases here described all evidence of the disease disappeared at least temporarily. One patient has remained free from recurrence for 3 years after the original resection and chemotherapy.—[Editorial summary.]

Infectious Diseases

530. **Antibiotics in Small Doses for the Common Cold**
J. M. RITCHIE. *Lancet* [*Lancet*] **1**, 618–621, March 22, 1958. 1 ref.

Investigations were carried out at the Public Health Laboratory, Birkenhead, on the supposition that symptoms in the later stages of the common cold are due not to the virus, but to the nasal and pharyngeal bacteria, which became relatively more virulent through depression of resistance by virus infection. During the autumn of 1956 specimens of saliva from 919 volunteers were cultured on blood agar and the sensitivity of the organisms to different antibiotics was assessed. In this way the most suitable of three antibiotics—tetracycline, oxytetracycline, and chlortetracycline—was determined for each individual. To those reporting prodromal symptoms of a cold 4 tablets, containing either 15 mg. of the appropriate antibiotic or glucose, were issued, 2 of which were taken on that day and 2 on the following day.

Of the 338 subjects used as controls, 182 (54%) reported during the initial stages of a cold and were given tablets containing glucose; of these, 87 developed full colds. Of the remaining 581 subjects, 287 (49%) had the prodromal symptoms of a cold and were given one or other of the antibiotics; only 20 of these developed symptoms of a full cold. The author therefore advocates treatment of colds in the prodromal or virus stage to prevent symptoms due to subsequent bacterial invasion.

R. Hare

531. **Some Aspects of the Recent Epidemic of Influenza in Dundee**
A COMBINED STUDY GROUP. *British Medical Journal* [*Brit. med. J.*] **1**, 908–913, April 19, 1958. 9 refs.

This is a report of the recent epidemic [October and November, 1957] of influenza in Dundee by a combined study group consisting of epidemiologists, clinicians, bacteriologists, and pathologists. During the six-weeks period beginning on October 1, 541 patients were admitted to hospital. There were 33 deaths. An analysis showed that the majority of those who died were aged 50 and over, and many had pre-existing disease of cardiac or respiratory nature.

Influenza virus A of the Asian type was isolated from selected cases. The demonstration of either a four-fold rise in titre or a significant initial titre of complement-fixing antibodies to influenza A virus was obtained in 70 out of 77 (91%) patients examined. Staphylococci were the most commonly isolated organisms from post-mortem material. In a proportion of cases the staphylococci were of the resistant type generally associated with hospitals.

Second attacks of influenza within a period of 7 weeks are reported. Attention is drawn to 2 cases of encephalitis which are possibly influenzal in origin. Measures for the treatment of influenzal pneumonia are discussed. A plea is made for further studies on the local epidemiology of influenzal pneumonia, especially from the point of view of the bacterial component.—[Authors' summary.]

532. **Deaths from Asian Influenza, 1957**
A REPORT BY THE PUBLIC HEALTH LABORATORY SERVICE BASED ON RECORDS FROM HOSPITAL AND PUBLIC HEALTH LABORATORIES. *British Medical Journal* [*Brit. med. J.*] **1**, 915–919, April 19, 1958. 2 figs., 1 ref.

Records of 477 patients who died from pneumonia in the 1957 epidemic of Asian influenza were obtained from laboratories throughout the country. Influenza virus A of Asian type was isolated from 195 of 310 specimens tested. The most striking feature of the illnesses was the speed with which the patients deteriorated and died after admission to hospital. The duration of illness increased with age; 60% of children under 5 died within 48 hours of onset, but only 10% of those over 45. Pneumonia—often haemorrhagic—tracheobronchitis, and lung abscess were the most frequent post-mortem findings.

Staphylococcus aureus was found in lung or sputum specimens from 62% of the patients. Other pathogenic organisms were reported in 8%, and the remainder yielded no pathogenic organisms or were sterile. Staphylococci were found less frequently in young children (49%) and old persons (31%); and most frequently in children of school age (88%). Although only 65% of staphylococci isolated from patients not admitted to hospital or dying within 48 hours of admission were sensitive to penicillin, most infections, except in old people, were acquired outside hospital.—[Authors' summary.]

533. **An Illness Resembling Acute Poliomyelitis Caused by a Virus of the Russian Spring–Summer Encephalitis/Louping Ill Group in Northern Ireland**
M. LIKAR and D. S. DANE. *Lancet* [*Lancet*] **1**, 456–458, March 1, 1958. 12 refs.

The authors report from the Queen's University of Belfast that in 1957 isolation of the virus from the faeces was attempted in all cases of paralytic poliomyelitis, aseptic meningitis, and encephalitis occurring in Northern Ireland. In 34 cases of paralytic poliomyelitis no virus could be isolated and it was decided to test the serum of these patients against the virus of Russian spring–summer encephalitis (R.S.S.E.), which is considered to be identical with the virus causing louping-ill in sheep. Positive results were obtained in 5 cases—4 of paralytic poliomyelitis and one of mild encephalitis—the results of complement-fixation tests being positive and the presence of neutralizing antibodies against R.S.S.E. virus also being demonstrated. In all of 100 cases of paralytic poliomyelitis in which the poliomyelitis virus was found the tests for R.S.S.E. virus gave negative results, while of

66 patients suffering from proven influenza, the complement-fixation test against R.S.S.E. was positive in 4, but in none of these could the presence of neutralizing antibodies be demonstrated.

A full clinical report is given of the 5 patients in the first group. One of these, a medical student, had been bitten 5 days before the onset of his illness by a tick, which he had preserved and which was later identified as *Ixodes reduvius*, the known transmitter of louping-ill among sheep; there was no information as to the mode of infection in the other 4 cases. The authors suggest that in future, in considering cases of paralytic infection, it will be important to exclude infection with the R.S.S.E. virus, especially in subjects who have been immunized with the Salk-type poliomyelitis vaccine. *John Fry*

534. **A Study of the Hearing Level following Severe Poliomyelitis**

R. BATSON and F. MCCONNELL. *A.M.A. Journal of Diseases of Children* [*A.M.A. J. Dis. Child.*] **95**, 139–145, Feb., 1958. 5 figs., 15 refs.

At Vanderbilt University School of Medicine and the Bill Wilkerson Hearing and Speech Center, Nashville, Tennessee, an audiometric survey has been made of 37 patients severely disabled by paralytic poliomyelitis, all of whom had moderate or severe respiratory failure. Comparative testing of normal subjects under similar conditions was also carried out. The patients showed an average loss of 13 decibels in all frequencies tested; characteristic was a flat loss with bone conduction equal to air conduction. In general, the greater loss of hearing was found in patients with the greater loss of vital capacity. *T. A. Clarke*

535. **Virus Diseases in Pregnancy and Congenital Defects**

A. BRADFORD HILL, R. DOLL, T. MCL. GALLOWAY, and J. P. W. HUGHES. *British Journal of Preventive and Social Medicine* [*Brit. J. prev. soc. Med.*] **12**, 1–7, Jan., 1958. 8 refs.

This paper from the Statistical Research Unit of the Medical Research Council gives the most authoritative estimates yet available of the risk of congenital malformations occurring in children whose mothers experienced certain virus diseases during pregnancy. By arrangement with the Ministry of Pensions and National Insurance details were obtained during the period November, 1949, to March, 1953, of those married women in certain localities of England and Wales who (1) claimed sickness benefit in respect of rubella, measles, chicken-pox, or mumps, and (2) within 12 months also claimed maternity benefit. They numbered 100 and, together with 22 obtained in a previous study (by similar methods) and 7 others notified privately, were followed up to determine the effects on the resulting children. With the cooperation of the general practitioners concerned the authors were able to visit and question the mothers. This led to the exclusion of 10 for various reasons, leaving 119 who gave birth to 120 children, 16 of whom were stillborn or died soon after birth. The authors examined most of the other children shortly after birth and again after they had reached their third birthday. The virus diseases which affected the 119 mothers during (or shortly before) the period of pregnancy were: rubella, 44; measles, 10; chicken-pox, 30; and mumps, 35. No abnormalities were found in the children of the 6 mothers who contracted rubella during the 3 months before pregnancy. The findings in the remaining cases of this disease were as follows.

Time of Attack (week of pregnancy)	No. of Mothers	Resultant Children			
		Congenital Malformation	Stillborn	Neonatal Death	Normal
0 to 4	7	3	—	—	4
5 to 13	11	1	—	1	9
14 to 23	15	1	1	1	12
27 or later	5	—	—	—	5
Total	38	5	1	2	30

Of the 36 children in this group who were normal on first examination, 33 were still normal at the later examination, one had died, and 2 could not be traced. All the remaining 8 children weighed less than 7 lb. (3·2 kg.) at birth. By combining these data with those from three other published series (the material of which satisfied certain criteria) the authors were able to estimate that where rubella occurs in the first lunar month of pregnancy the risk of giving birth to a child with a congenital defect is 50%. This chance declines to 25% if the attack occurs in the second month, to 17% in the third, to 11% in the fourth, and to 6% in the fifth and sixth months. The children of mothers attacked after the 24th week seem to be unaffected. The over-all incidence of congenital malformations in live births was 12% (5 amongst 43 live births), which is about four times greater than the accepted rate for the general population. [The abstracter, with Grundy, found a rate of 2·9% in a study of 20,000 live births.]

There was no conclusive evidence that measles, mumps, or chicken-pox in the mother before or during pregnancy had any association with the occurrence of congenital defects. Thus of the children of 10 mothers contracting measles (shortly before pregnancy in 4 cases), 2 showed congenital defects; of the children of 35 mothers attacked by mumps, one had evidence of bilateral talipes equinovarus and another died aged 3 days, though necropsy revealed no specific defect; and of the 31 children born to 30 women attacked by chicken-pox, one had an isolated defect of pancreatic secretion and 2 were stillborn.

The authors stress that their inquiry was limited to the effect of attacks of these diseases during pregnancy on the occurrence of congenital malformations in live and stillbirths, and that "if virus diseases in pregnancy contribute to early foetal loss this inquiry cannot reveal it". *E. Lewis-Faning*

536. **The Chemotherapy of Helminthiasis.** [Review Article]

T. I. WATKINS. *Journal of Pharmacy and Pharmacology* [*J. Pharm. (Lond.)*] **10**, 209–227, April, 1958. Bibliography.

Tuberculosis

537. **Tuberculosis in the Neonatal Period**
E. L. KENDIG and W. L. RODGERS. *American Review of Tuberculosis and Pulmonary Diseases* [*Amer. Rev. Tuberc.*] **77**, 418–422, March, 1958. 5 refs.

The authors, from the Department of Pediatrics and the Child Chest Clinic, Medical College of Virginia, Richmond, report a study of 60 infants born to mothers who had active pulmonary tuberculosis at the time of delivery or had recently had active disease, or who contracted active tuberculosis while the child was in infancy. Of the 60 infants, 9 received B.C.G. vaccination; none of these developed clinical evidence of tuberculosis. Three infants had no contact with the mother and remained free from the disease. Of the remaining 48, 21 became infected, although in only 7 instances was the mother found to have a positive sputum; examination of household contacts revealed no other source of tuberculous disease. In all except 3 of the infected children there was clinical or radiological evidence of tuberculosis; the 3 exceptions gave a positive reaction to the Mantoux test. The majority of infected infants had been in close contact with their mothers, but severe tuberculosis developed in 2 who had been in contact only during the first day of life. Two infants escaped infection in spite of intimate exposure to the mother. Of 10 infants who were separated from their mothers at birth for periods ranging from 7 weeks to 2 years or until the disease in the mother was arrested, 6 were infected.

C. M. Fletcher

538. **Freeze-dried B.C.G. Vaccine. Results of Laboratory Tests and of Trials among Schoolchildren in Middlesex**
A PRELIMINARY REPORT TO THE MEDICAL RESEARCH COUNCIL BY THEIR COMMITTEE ON THE STANDARDIZATION OF FREEZE-DRIED B.C.G. VACCINE. *British Medical Journal* [*Brit. med. J.*] **1**, 79–83, Jan. 11, 1958. 7 figs., 7 refs.

In a previous report to the Medical Research Council (*Brit. med. J.*, 1956, **1**, 413; *Abstr. Wld Med.*, 1956, **20**, 102) the trial of a Danish liquid B.C.G. vaccine was described. In the present paper a trial of a British freeze-dried B.C.G. vaccine is reported. As a preliminary to the trial, viable counts were made both on the Danish liquid vaccine and on the reconstituted freeze-dried vaccine, since it is well known that the viable count in different batches of any B.C.G. vaccine may vary considerably. Although it was not possible to compare the counts in the two vaccines directly, as they are manufactured by fundamentally different processes, the number of viable bacillary particles in successive batches of each type of vaccine was found to be within reasonably constant limits.

Four batches of the freeze-dried vaccine and 15 batches of the liquid vaccine were then selected for use in the trials. These were carried out on 4,293 tuberculin-negative school-children aged 13 and 14 from six areas in the County of Middlesex who were given one or other of the vaccines by random selection according to the month of birth, 2,242 receiving the liquid vaccine and 2,051 the dried vaccine. Tuberculin tests with 3 t.u. and 100 t.u. were repeated and the vaccination site inspected in some of the children at 5 to 7 weeks and in the remainder at 10 to 17 weeks. Comparison of the results was made in the following respects: (1) the percentage of children giving a positive reaction (diameter of induration greater than 5 mm.); (2) the mean diameter of this reaction; and (3) the mean diameter of the local vaccination lesion. The conversion rate found at 5 to 7 weeks was 90·5% for those given the dried vaccine and 97·1% for those given the liquid vaccine (among 687 and 780 children respectively completing the tests); corresponding figures at 10 to 17 weeks were 90·3% and 95·5% respectively (1,085 and 1,149 children respectively). All the children in both groups who were negative to 3 t.u. subsequently reacted to 100 t.u. This is considered to be satisfactory, as previous work has shown that a conversion rate of 86% gives a high degree of protection against tuberculosis. It is pointed out, however, that the present trial was not designed to assess the value of the dried vaccine in the prevention of tuberculosis. Until further tests of the keeping qualities of the vaccine are completed it is recommended that the dried vaccine be kept in a refrigerator until required.

John M. Talbot

RESPIRATORY TUBERCULOSIS

539. **Endobronchial Tuberculosis in Children. A Study of 156 Patients**
E. M. LINCOLN, L. C. HARRIS, S. BOVORNKITTI, R. W. CARRETERO. *American Review of Tuberculosis and Pulmonary Diseases* [*Amer. Rev. Tuberc.*] **77**, 39–61, Jan., 1958. 8 figs., 28 refs.

In a previous paper from Bellevue Hospital (New York University College of Medicine), New York (*Amer. Rev. Tuberc.*, 1954, **69**, 682; *Abstr. Wld Med.*, 1954, **16**, 371) based on the observation of almost 1,000 children with primary pulmonary tuberculosis between 1930 and 1946 it was shown that although the disease was infrequently fatal, permanent bronchial or pulmonary damage due to endobronchial involvement was fairly common, as numerous other investigators have found. The present paper reports the results of further observations designed to assess the influence of treatment with specific antituberculous drugs upon endobronchial disease and its late effects in children.

The patients selected for study were children with symptoms suggesting endobronchial tuberculous disease or *x*-ray evidence of bronchial obstruction, together with a

few others with tubercle bacilli persistently present in the gastric washings despite the absence of symptoms and *x*-ray abnormalities. Up to July, 1954, 156 of these children were found to have bronchoscopic evidence of endobronchial tuberculosis. The most frequent bronchoscopic finding was granulation tissue. Polyps were present in 54 cases and erosion of the bronchial wall in 25. Of these 156 children, 83% were under 4 years of age (compared with 65% of the total ward population of tuberculous children) and 60% were males. Severe symptoms were most common in infants. *X*-ray evidence of segmental obstruction was found in 90%, being most common in the right middle lobe and the anterior segment of the right upper lobe. Bronchography was performed in 103 cases and revealed abnormalities in 70, bronchiectasis being the most common and most severe. Antituberculous drugs (streptomycin, PAS, isoniazid, and sulphones in various combinations) were given to 77% of the children—to 66% for more than 6 months and to 48% for more than a year. [Precise details of dosage are not given.]

No evidence was found to suggest that treatment with antituberculous drugs significantly shortened the course of tuberculous endobronchitis in children, although in adults tuberculous endobronchial disease generally responds to chemotherapy. The authors suggest that the difference in response may be readily explained by differences in pathogenesis, bronchial tuberculosis in adults being usually a superficial lesion due to contamination of the mucosal surface by tubercle bacilli from an adjacent cavity, whereas in children it results from encroachment on the bronchial wall by a caseous lymph node, the infection progressing through all the layers of the wall to the mucosa. The basic lesion in the latter case is thus in the lymph node, and there is some evidence that tuberculosis in lymphatic tissue responds less well to antituberculous drugs than it does in other sites. The incidence of irreversible damage to the bronchi and lung tissue also appeared to be uninfluenced by specific drug therapy, resection of a lung or segment being necessary in 10 cases.

Despite these findings the authors consider that antituberculous drugs should always be used in the treatment of tuberculous endobronchitis in children, if only to lessen the danger of bronchogenic spread.

Raymond Parkes

540. **Nontuberculous Pneumonia Complicating Pulmonary Tuberculosis**

S. A. LABARBERA, H. H. EPSTEIN, L. L. FULKERSON, and A. S. GRANSTON. *Annals of Internal Medicine* [*Ann. intern. Med.*] **48**, 635–646, March, 1958. 10 refs.

This paper from the U.S. Public Health Service Hospital, Manhattan Beach, Brooklyn, describes the characteristics of non-tuberculous pneumonia occurring in the course of pulmonary tuberculosis as seen in a series of 47 cases in 36 patients, with no deaths. During the period of the study (1945 to 1955 inclusive) a total of 2,769 patients with pulmonary tuberculosis were admitted on one or more occasions to the hospital, most of them being merchant seamen with a high incidence of alcoholism. The 36 patients with pneumonia were all male, their ages ranging from 40 to 69 years. The tuberculosis was minimal in 2 cases and in 55% was considered to be inactive by the criteria of the National Tuberculosis Association. In 68% of the cases the patient was not receiving specific antituberculous treatment, and in 72% he was on pass or was not hospitalized, at the time of onset of the pneumonia.

Fever, chest pain, and chills were the major symptoms. The *x*-ray appearances were those of lobar pneumonia in 8 cases, lobular pneumonia in 26, and diffuse bronchopneumonia in 13. In 33 of the 34 cases of localized pneumonia the signs were confined to the lower and middle lobes. Of the 29 cases in which sputum smears were examined and cultures made, pneumococci were isolated definitely in 8 and probably in 2. Typing sera were not available. Only in one case did demonstrable activation of the tuberculosis by the pneumonia occur, new infiltration occurring in the same area as the pneumonia in a case of sputum-positive tuberculosis involving other segments of the same lobe. Bronchoscopy or bronchography or both was carried out in 18 cases, in 11 of which some tracheobronchial abnormality was found in the pneumonic area on bronchoscopy, while in 5 bronchial distortion was demonstrable on bronchography.

It is pointed out that in most of these cases the pneumonia developed outside hospital, the incidence of complicating non-tuberculous pneumonia being considerably less among patients in hospital. Nevertheless, the authors emphasize that the possibility of concurrent pneumonia should be kept in mind in any case of chronic tuberculosis in which a new area of patchy infiltration appears.

I. M. Librach

541. **The Effect of Chemotherapy of Patients with Open Pulmonary Tuberculosis on the Tuberculous Contamination of the Home Environment.** (L'incidence de l'antibiothérapie des cracheurs de bacilles de Koch sur la contamination tuberculeuse au foyer)

A. LEVI-VALENSI, A. ASPAR, and S. GHENASSIA. *Presse médicale* [*Presse méd.*] **66**, 341–343, Feb. 26, 1958. 5 figs., bibliography.

In this communication from the Faculty of Medicine, Algiers, the authors first discuss the divergent opinions that have been expressed on the value of chemotherapy in reducing the number of contact cases of pulmonary tuberculosis in the home. In order to throw further light on this problem they have investigated 200 Algerian homes in which there was a tuberculous patient whose sputum was positive for tubercle bacilli; in half the homes the index patient received no antituberculous chemotherapy, whereas in the remaining half he was given isoniazid. It was found that in the former group of households 40% of the contacts became infected, whereas in those in which the patient received treatment the corresponding figure was only 9%. Of the 100 patients receiving treatment, the sputum did not become negative in 11 and this small group accounted for an appreciable proportion of the infected contacts in the homes of these patients. It was noted that patients who had had previous treatment in hospital were less danger-

ous to their contacts than those who had received only domiciliary chemotherapy. The authors have also been impressed by the value of the extensive B.C.G. campaign carried out in Algeria.

[It would appear from this paper that in Algiers isoniazid is still being used by itself, contrary to all teaching in Great Britain and elsewhere.] *Paul B. Woolley*

542. **Extrapleural Thorocoplasty in the Treatment of Pulmonary Tuberculosis. An Eight- to Twenty-one-year Follow-up Study**
M. S. HARTE and A. H. AUFSES. *Journal of Thoracic Surgery* [*J. thorac. Surg.*] **35**, 332–340, March, 1958. 2 figs., 2 refs.

Between 1935 and 1947 at Montefiore Hospital, New York, thoracoplasty was performed on 180 patients suffering from pulmonary tuberculosis, and in this paper the follow-up results 8 to 21 years after operation are reported. There were 9 postoperative deaths, 3 being due to a pleural tear, 1 to suppuration, 1 to massive contralateral collapse, 1 to an unsuspected phaeochromocytoma, and 1 to shock. In 2 cases no cause for death was found. There were 35 further deaths in the series, 20 of which were due to tuberculosis; in 15 cases death was due to causes other than tuberculosis, but in 5 of them the disease was still active at the time of death. Of the remaining 136 cases in the series, 7 required further surgical treatment before the disease became quiescent and in 6 active disease was still present. Excluding the postoperative deaths, thoracoplasty was unsuccessful in 38 out of 171 cases.

The causes of failure of thoracoplasty included the presence of contralateral disease, giant cavities, middle- or lower-lobe cavities, and endobronchial disease, and also delay between the stages of thoracoplasty. The authors point out that with improved surgical and anaesthetic technique and chemotherapy many of these hazards would now be avoided. They consider that thoracoplasty will achieve a cure in a high proportion of suitable cases and should not be discarded in favour of resection. *L. Capper*

543. **The Treatment of Patients with Tuberculosis of the Bronchi and Lungs by Intratracheobronchial Introduction of Antibiotics.** (Лечение интратрахеобронхиальным введением антибиотиков больных туберкулезом бронхов и легких)
M. V. ŠESTERINA. *Проблемы Туберкулеза* [*Probl. Tuberk.*] **36**, 55–61, No. 2, 1958.

The introduction of medicinal substances directly into the respiratory tract has been known since the days of Hippocrates, but is generally used only by veterinary surgeons. The procedure can be carried out in several ways: (1) by transtracheal puncture, but this method is not recommended on account of possible complications such as emphysema or damage to the thyroid gland; (2) by inhalation of the pulverized substance, which, however, has the disadvantage that more than 60% of the drug may be lost; (3) through a bronchoscope, but this method should be used only when bronchoscopy is indicated; (4) by means of a catheter introduced through the nose and the larynx—a complicated process which may irritate the mucous membrane and cannot be used more than 2 or 3 times a week; (5) by injection into the larynx with a syringe. This is the method recommended by the author. The patient is instructed to breathe slowly and deeply and to relax completely, and sometimes local analgesia of the pharynx is necessary; during the procedure the patient is turned first to the right and then to the left side.

The present report is based on the results obtained in 93 patients with chronic pulmonary tuberculosis who were given intratracheal injections of streptomycin and "salucide" during 1954 and 1955, in most cases mainly for the relief of intractable cough; for this purpose the treatment gave "remarkable results". The daily number of injections varied from 10 to 40, but was usually about 25. The method was employed as an adjunct to the general treatment of the tuberculosis. Of the author's patients, 11 of whom were aged over 50, 58% suffered from chronic fibrous-cavernous tuberculosis, 5% from chronic disseminated tuberculosis, 6% from focal tuberculosis, and the remainder from non-effective artificial pneumothorax. Clinical cure was achieved in 64 cases and considerable improvement in a further 19.

H. W. Swann

544. **The Bacteriology of Tuberculous Lesions Resected after Chemotherapy**
R. G. BLOCH, A. S. BUCHBERG, S. PERMUTT, and G. NEUMANN. *American Review of Tuberculosis and Pulmonary Diseases* [*Amer. Rev. Tuberc.*] **77**, 245–259, Feb., 1958. 10 refs.

Advances in thoracic surgery have opened the way to the detailed pathological and bacteriological study of pulmonary tuberculous lesions removed from the living patient, and in the present study, carried out at the Montefiore Hospital, New York, an attempt was made to correlate the bacteriological findings in such resected lesions with (1) the preoperative findings in the sputum, (2) the type of lesion, and (3) the duration of preoperative chemotherapy. The study was based on the examination of 400 different tuberculous lesions obtained from 81 patients subjected to segmental resection, lobectomy, or pneumonectomy. The pathological observations were limited to gross inspection of the specimen.

Results showed that chemotherapy did not have as much influence on cavity behaviour as has been claimed hitherto. Caseation was present in the majority of all types of lesion. About 69% of large open cavities yielded positive cultures, while 56% of medium-sized and only 34% of small cavities did so. Cavities generally gave a higher incidence of positive cultures (52·5%) than closed lesions (37·5%). Smooth-walled cavities were seen only on 4 occasions, but viable bacilli were recovered from 2 of these. Bacilli were grown almost as frequently from small as from large closed tuberculous nodules. In satellite lesions the bacteriological findings were similar to those in the main lesions. It was significant that 42·5% of lesions from "sputum-negative" patients gave positive cultures, although some of these patients had shown sputum conversion during chemotherapy. Prolongation of preoperative chemotherapy

beyond 6 months resulted in a higher incidence of positive cultures, a finding which is attributed to the emergence of resistant strains of tubercle bacilli. It is considered that the optimum time for surgical resection lies within the first 6 months of chemotherapy. The essential bacteriological findings are presented in a series of 14 tables. [For details the original paper should be consulted.]

E. G. Rees

EXTRA-RESPIRATORY TUBERCULOSIS

545. **Sterilization of the Lesions of Bone and Joint Tuberculosis by Antibacterial Chemotherapy.** (Stérilisation des lésions de la tuberculose ostéo-articulaire par la chimiothérapie antibacillaire)

G. CANETTI, J. DEBEYRE, and S. DE SÈZE. *Revue de la tuberculose* [*Rev. Tuberc. (Paris)*] **21**, 1337–1344, Dec., 1957 [received April, 1958]. 9 refs.

In this study 87 specimens removed at operation from 76 patients with tuberculous disease of bones or joints were examined for tubercle bacilli by culture and direct microscopical examination; the sensitivity of the organisms to chemotherapeutic agents was also investigated. Of the 19 specimens obtained within one month of chemotherapy being started bacilli were found in 18 (95%), of 22 taken during the second month of chemotherapy positive cultures were found in 12 (55%), while after 2 months or more of treatment cultures were positive in only 9 out of 35 specimens (26%). This progressive sterilization of the lesion was also associated with a reduction in the number of colonies in those cultures which were still positive. Studies of drug resistance indicated that 42 out of 44 of the cultures remained sensitive to all the three antituberculous drugs used, namely isoniazid, PAS, and streptomycin. *Peter Ring*

546. **Tuberculous Meningitis in Children Treated with Isoniazidmethanesulfonate**

H. YOSHIDA and K. YANAGAWA. *Journal of Pediatrics* [*J. Pediat.*] **52**, 289–294, March, 1958. 2 figs., 11 refs.

The authors, from the Department of Paediatrics, University of Tokyo, report a trial of a derivative of isoniazid, isoniazidmethanesulphonate (IHMS), in the treatment of 10 children with severe tuberculous meningitis. This compound was not toxic, and dose for dose with isoniazid it produced a similar maximum concentration in the blood, although the highest level was attained more slowly than the highest concentration of isoniazid. After oral administration the blood level of this compound fell less rapidly than that of isoniazid. There was a good concentration in the cerebrospinal fluid, even in healthy subjects.

The cases were selected for treatment because of prolonged unconsciousness, delay in the institution of treatment, or recurrence of attacks in spite of treatment with streptomycin and isoniazid. In 6 of the cases the daily dosage of the compound exceeded 30 mg. per kg. body weight for periods varying between 4 months and one year; in one case the maximum daily dose was as high as 150 mg. per kg. body weight. Streptomycin and PAS were given in addition. IHMS was also administered intrathecally [but it is not clear how often or to how many patients]. Of the 10 children, 7 recovered (one with residual paralysis) and 3 died. [There were no infants in the series.] *John Lorber*

547. **Radiological Techniques in the Management of Tuberculosis Meningitis**

R. M. ACHESON and H. V. SMITH. *Quarterly Journal of Medicine* [*Quart. J. Med.*] **27**, 83–101, Jan., 1958. 13 figs., 21 refs.

The value of radiological techniques in the management of tuberculous meningitis is discussed with reference to 313 cases treated between 1946 and 1955 either at the United Oxford Hospitals or at the Military Hospital for Head Injuries, Wheatley, Oxfordshire. Techniques suitable for introducing small amounts of air into the cerebrospinal-fluid pathways are described. The lumbar or cisternal route is used, without general anaesthesia and with the minimum of discomfort to the patient.

In the earliest stages of the disease the only detectable abnormality in the air encephalogram may be a mild symmetrical dilatation of the ventricles, which shows as a blunting of the angles of the frontal horns in the postero-anterior view. Slight as this change may be, it can be helpful in the differential diagnosis of tuberculous meningitis from virus infections. As the disease evolves, the ventricles become larger and the air encephalogram diverges farther and farther from the normal. The authors' conclusions may be summarized as follows. Although improvement or deterioration in the appearance of the air encephalogram is always accompanied by a comparable change in the patient's clinical condition, recovery may take place without any change in the encephalogram. "If a small quantity of air which has been introduced into the lumbar theca fails to enter the skull on more than one occasion, it is a reliable sign that a spinal block exists. If air fails to pass from the cisterna magna into the ventricular system on more than one occasion, it suggests a lesion at the outlet of the fourth ventricle. Resolution of basal exudate has been demonstrated in patients who have been treated with the purified protein derivative of tuberculin (P.P.D.). Such resolution was unknown when intrathecal streptomycin was the sole form of therapy and this evidence strengthens [the authors'] opinion that P.P.D. is a necessary adjuvant to daily intrathecal streptomycin and isoniazid. . . .

"Major degrees of hydrocephalus are characteristic of the more severe cases, particularly in childhood. Although gross hydrocephalus usually carries a poor prognosis, it can be followed by a useful intellectual recovery, even in children. Cerebral angiography has not proved to be of assistance in the management of tuberculous meningitis . . . Myelography [with iodized oil] is of value in distinguishing the exudative spinal block of tuberculous meningitis from obstruction of the spinal cord due to a collapsed vertebra or neoplasm."

Intracranial calcification was seen in 15 of 104 cases followed up for two years after the start of treatment.

J. MacD. Holmes

Venereal Diseases

548. **Common Contagious Genito-urinary Diseases with Reference to the Ito–Reenstierna and Frei Tests**
D. E. TYLER. *British Journal of Venereal Diseases* [*Brit. J. vener. Dis.*] **33**, 228–241, Dec., 1957. 39 refs.

As a result of his experience as medical officer on a troopship operating between the U.S.A. and Japan the author concludes that there is considerable doubt as to the accuracy of the diagnosis of chancroid which is frequently made on ulcerative penile lesions, basing this conclusion on an investigation into the characteristics of the lesions and the reactions obtained to the Ito–Reenstierna (I.R.) and Frei tests. Of almost 200 patients seen with ulcerative penile lesions with or without adenitis, only 10% gave positive I.R. reactions. None of the control subjects had positive reactions. Similarly all tests with the Frei antigen gave negative results. These last observations, it is pointed out, are contrary to those reported by other investigators. It was further observed that the presence, or a past history of, non-specific penile lesions tended to make the local tissue test reaction slightly more extensive than in non-infected controls, although it was still within the normal range. Smallpox vaccination carried out at the time of testing caused a similar response. The author suggests that most of the penile lesions seen in this study were those of herpes genitalis, which presents a clinical picture of ulcerative or herpetiform lesions of the penis with little local tissue destruction or inguinal adenitis.

[This paper demonstrates well the futility of diagnosing penile or intra-urethral chancroid on the basis of morphological appearance or staining reactions of organisms present alone.] *Allene Scott*

549. **Gonorrhoea in Manchester. Incidence of Repeated Infections**
L. WATT. *British Journal of Venereal Diseases* [*Brit. J. vener. Dis.*] **34**, 9–13, March, 1958. 2 refs.

Since the introduction of penicillin therapy for venereal disease it has become increasingly apparent that reinfections account for a considerable proportion of the cases of gonococcal infection reported in large urban areas in Britain, particularly those areas which include homeless, male immigrants from the Carribean and West Africa and male casual workers from Eire. Greater Manchester, which has an estimated population of 2,400,000, including some 8,000 West Indians, is served by a number of V.D. clinics, and in the present paper the incidence of reinfections among patients treated at one of these, St. Luke's Clinic, is discussed.

Of 1,482 male patients treated for gonorrhoea during the two years 1955 and 1956, 810 (54·6%) were suffering from a first infection and 672 (45·4%) admitted having had a previous attack. Of 1,287 patients whose nationality was known, 597 (46·4%) came from overseas: in fact over half (54·1%) of the infections treated in the clinic in 1956 occurred among immigrants. The percentage distribution of the 1,482 patients according to nationality was as follows: United Kingdom 53·6; Carribean 13·1; Eire 12·1; West African 10·6; all others 10·1. As expected, reinfections occurred relatively more often among the coloured patients, one patient from West Africa and two from the Carribean each having a total of 8 separate infections for which they were treated at St. Luke's Clinic during 1956.

The author considers that a more accurate picture of the incidence of gonorrhoea would be obtained if the returns showed the number of individuals affected as well as the total number of infections they contracted.
G. L. M. McElligott

550. **Antibiotic Quarantine of Gonorrhoea. I. Effect in Females**
I. L. SCHAMBERG, A. KALODNER, and J. W. LENTZ. *British Journal of Venereal Diseases* [*Brit. J. vener. Dis.*] **34**, 24–30, March, 1958. 2 figs., 26 refs.

Although the introduction of penicillin has produced a striking decline in the number of cases of early syphilis, a similar reduction in the incidence of gonorrhoea has not been achieved and there has been a failure to control this disease. During the period 1956–7 the authors, working in the Department of Public Health, Philadelphia, have attempted to meet this situation by treating approximately 2,400 male and 1,700 female patients with 2·4 mega units of benzathine penicillin with the object of securing a " quarantine " serum penicillin level which would render the patient unable to contract or transmit gonorrhoea for a period of approximately 8 weeks. At the end of this time all female patients were asked to return for further similar treatment. Only 2% failed to accept at least one re-treatment, while 43% submitted to 2 to 4 re-treatments. Thus the period of " antibiotic quarantine " was prolonged beyond 2 weeks in a significant proportion of cases.

Gonococci were demonstrated in cervical or urethral smears from 9 females and 6 males within 8 weeks after the first treatment, indicating a failure rate of 0·5% in females and 0·25% in males. It is stated that benzathine penicillin in a dose of 2·4 mega units produces a blood level of antibiotic during 50 or more days after the injection which is sufficiently high to kill 95% of strains of gonococci, but is rarely sufficient to kill the most resistant strains. In order to prevent the dissemination of such strains a preparation of penicillin producing a higher initial blood level is desirable, and a mixture containing 600,000 units of aqueous procaine penicillin and 1·2 mega units of benzathine penicillin is now being used by the authors in their most recent gonorrhoea control programme. *R. R. Willcox*

SYPHILIS

551. **Saturated Synthetic Lecithins in VDRL and Kolmer Antigens for the Serodiagnosis of Syphilis**
D. B. TONKS and R. H. ALLEN. *British Journal of Venereal Diseases* [*Brit. J. vener. Dis.*] **33**, 249–257, Dec., 1957. 19 refs.

Writing from the Department of National Health and Welfare, Ottawa, the authors recall that the availability of pure individual synthetic lecithins to replace the Pangborn lecithin in cardiolipin antigen has permitted more extensive studies of the reliability of the former and their ability to replace the older material. Distearoyl-lecithin (DSL) was early discarded because of its limited solubility, and most of the studies here described were performed with dipalmitoyl-lecithin (DPL) and dimyristoyl-lecithin (DML). The method used was that employed in the U.S. Public Health Service, modified, however, by heating the antigen suspensions for 5 minutes at 56° C. shortly after preparation.

Both DPL and DML formed good flocculates, but those with the former were slightly atypical and the authors therefore prefer DML for most purposes. Serological comparisons with the standard V.D.R.L. and Kolmer test antigens showed that the saturated lecithin antigens were slightly more sensitive than the standard ones, but sufficient material was not yet available for studies of reproducibility. For the V.D.R.L. antigen the composition was 0·03 cardiolipin, 0·3 DML, and 0·9 cholesterol, expressed as concentrations in g. per 100 ml.; for the Kolmer antigen the corresponding concentrations were 0·0175, 0·225, and 0·3 respectively. It is concluded that if the results are adequately reproducible the advantages of stability, solubility, and more ready control of sensitivity seem to suggest that these new synthetic forms of lecithin could replace the Pangborn lecithin.

Allene Scott

552. **Neurosyphilis and Penicillin. Some Problems of Diagnosis, Prognosis, and Treatment.** (Sífilis nerviosa y penicilina. Algunos problemas diagnósticos, pronósticos y terapéuticos)
T. ORBÁN. *Acta neuropsiquiátrica argentina* [*Acta neuropsiquiát. argent.*] **3**, 341–346, Oct.–Dec., 1957. 37 refs.

From the Institute of Venereology, Budapest, the author presents the results of treatment in 512 cases of neurosyphilis, these comprising 227 cases of meningovascular syphilis, 103 of asymptomatic neurosyphilis, 81 of tabes dorsalis, 40 of general paralysis, and 61 of taboparesis, all of which were discovered as a result of the examination of 5,000 syphilitics. The importance of examining the cerebrospinal fluid (C.S.F.) in all cases of latent syphilis before treatment is instituted is stressed.

Findings in the C.S.F. are presented in tabular form, using the classification of Moore. In 35% of cases of tabes routine examination of the C.S.F. gave negative results, but in these the treponemal immobilization reaction was positive. Results are given for the entire group of 512 patients, including those treated by various methods before the advent of penicillin, and also for the 344 (67%) amongst them who received the antibiotic. Penicillin was used in the form of "supracillin" (procaine penicillin with aluminium monostearate in oil) or "bismocillin" (procaine penicillin with aluminium monostearate and bismuth subsalicylate). Patients first received 2 or 3 courses each of 6 to 9 mega units, and if after an interval [duration not stated] the C.S.F. still showed evidence of activity a further course of penicillin was given. If this, too, was unsuccessful it was repeated, with the addition of fever therapy. The author concludes that penicillin is required in 67% of cases of neurosyphilis and that all cases in which there is clinical or serological activity should be treated initially with penicillin alone.

[It seems likely that the outcome, in terms of the reversion of changes in the C.S.F., has been assessed prematurely in this series. Hahn and co-workers (*J. chron. Dis.*, 1958, **7**, 209, and *A.M.A. Arch. Derm.*, 1956, **74**, 355, and 367; *Abstr. Wld Med.*, 1957, **21**, 249) have shown that changes in the C.S.F. may take a considerable time to subside following the successful treatment of neurosyphilis.] *Eric Dunlop*

553. **Differentiation of the Antilipids Occurring in Nontreponemal Diseases and Syphilis**
J. F. KENT, J. C. BURKE, D. P. CARROLL, L. A. SIMONTON, and A. GARCIA OTERO. *Journal of Chronic Diseases* [*J. chron. Dis.*] **7**, 36–42, Jan., 1958. 19 refs.

The authors, working at the Walter Reed Army Institute of Research, Washington, D.C., have studied the effect of varying the lecithin content of cardiolipin antigens used in the V.D.R.L. slide test and the Kolmer complement-fixation test. It was found that in both these tests reactivity with syphilitic sera was increased by increasing the lecithin content of the antigen, while reactivity with sera which otherwise gave non-specific reactions was decreased or abolished.

A simple test for the differentiation of the antilipid antibodies found in syphilis from those occurring in nontreponemal diseases, based on these observations, is described. Two sets of serial twofold dilutions of the serum under investigation from 1:1 up to 1:32 are made in triethanolamine buffered saline solution at *p*H 7·3 and are tested by the V.D.R.L. slide technique: (*a*) with V.D.R.L. antigen (which contains 0·15 g. of lecithin per 100 ml.), and (*b*) with a similar antigen containing 0·27 g. of lecithin per 100 ml., the concentrations of the other components being unchanged. Values ranging from ½ to 4 are allotted to the degrees of flocculation produced in each series, these values for each antigen being added together and the totals compared. The serological pattern is designated "non-syphilitic" if the V.D.R.L. antigen gives the greater total ("maximal reactivity"), "syphilitic" if the antigen with the increased lecithin content gives the greater total, and "equivocal" if the totals show a difference of no more than 1½, based on at least two serum dilutions.

This test was performed on sera from 119 cases in which the diagnosis of syphilis had been confirmed by positive dark-ground findings or positive reactions to specific treponemal tests, such as the treponemal im-

mobilization (T.P.I.) test. The pattern was syphilitic in 113, equivocal in 4, and non-syphilitic in 2 cases, these last 2 sera coming from patients with secondary and latent syphilis respectively. The test was also performed on 45 sera which were regarded as having given non-specific reactions in standard serological tests, the specific treponemal reactions being negative; in 38 of these cases the pattern was non-syphilitic, in 3 equivocal, and in 4 syphilitic. *A. E. Wilkinson*

NON-SPECIFIC URETHRITIS

554. **The Course of Reiter's Syndrome**
G. W. Csonka. *British Medical Journal* [*Brit. med. J.*] 1, 1088–1090, May 10, 1958. 1 fig., 6 refs.

The study herein reported is based on 185 consecutive patients (182 males and 3 females) suffering from Reiter's syndrome seen at St. Mary's Hospital, London, from 1942 to 1956 inclusive. During the same period 22,010 cases of urethritis were treated, so that the incidence of Reiter's syndrome in relation to the total number of urethral infections was 0·8%. Sexual promiscuity was apparent in the majority of patients, and there was usually a history of casual sexual relationship before the onset of the urethritis of Reiter's syndrome. In 87 cases this was associated with arthritis only, and in 98 there were other features, mainly eye and skin lesions. The age at onset ranged from 15 to 59 years, but 82% of the patients were in the age group 20 to 40 years. The mean duration of the attack in 165 cases was 3·8 months; in the remaining 20 cases no clear-cut remission was noted for 3 or more years. A total of 80 patients defaulted within one year, but of the remainder, some 50% were known to have had repeated attacks or continued activity over a number of years. In all, 30 patients were observed for 10 years or longer from the onset of the illness. It was noted that reinfection with venereal urethritis did not inevitably precipitate a fresh arthritic attack. With repeated attacks recovery became less complete, and some degree of permanent damage was evident in 28 patients. The author states that the various components of the syndrome need not occur simultaneously and that dissociation of symptoms is common.

No precipitating factor other than urethral infection was identified with certainty, but it is suggested that there may be a hereditary predisposition to the syndrome.
Leslie Watt

555. **Epidemiology of Non-specific Urethritis**
J. T. Boyd, G. W. Csonka, and J. K. Oates. *British Journal of Venereal Diseases* [*Brit. J. vener. Dis.*] **34**, 40–43, March, 1958.

As part of the study of the epidemiology of non-specific urethritis (N.S.U.) being carried out under the aegis of the Medical Research Council a comparison was made of various characteristics of 200 cases of first attacks of this disease with those of 200 cases of gonorrhoea seen at the Venereal Diseases Clinics of the London Hospital and St. Mary's Hospital, London.

There was no material difference in the incidence among patients aged under 40, but above this age the proportion of patients with N.S.U. was slightly higher (17% compared with 10%). Clinical signs revealed some differentiation, cases of N.S.U. presenting with a slight, thin, white discharge, as opposed to the profuse, thick, yellow discharge of gonorrhoea. The symptoms of N.S.U. were less severe and this was responsible for a longer history before first attendance—in a few cases as long as 6 weeks. Inquiry showed that 78% of patients with N.S.U. had a history of recent extramarital exposure in contrast to 96% of those with gonorrhoea, intercourse with a prostitute or casual woman acquaintance being admitted by 106 patients with N.S.U. and by 148 with gonorrhoea. A history of regular masturbation was obtained from 51 patients with N.S.U. compared with 27 with gonorrhoea. There appeared to be great variation (1 to 91 days) in the incubation period of N.S.U., and there was no definite peak to compare with the peak period of 3 to 4 days for gonorrhoea. No evidence was found that alcohol played any significant role in the causation of N.S.U., nor did locally applied chemicals, the use of contraceptive sheaths, or previous administration of antibiotics appear to be an aetiological factor.

It is concluded that the lack of any clear-cut pattern of behaviour of N.S.U. as compared with gonorrhoea suggests that this disorder is due to a number of different causes. *V. E. Lloyd*

556. **Furacin Urethral Suppositories in the Treatment of Non-gonococcal Urethritis. Further Observations.** [In English]
R. R. Willcox. *Acta dermato-venereologica* [*Acta derm.-venereol.* (*Stockh.*)] **38**, 68–77, 1958. 2 refs.

The author reports, from St. Mary's Hospital, London, additional observations on the results obtained with urethral suppositories containing 0·2% nitrofurazone and a local anaesthetic in a water-dispersable base (" furacin ") in the treatment of non-gonococcal urethritis. Of the 23 male patients, 9 had acute or subacute (not necessarily severe) urethritis and 14 had chronic urethritis. The suppositories were inserted twice a day for a period of 1 to 3 weeks. No intolerance was observed.

The case histories are described and the results of treatment summarized. In 4 cases the treatment failed, and in 5 of the remaining 19 there was a relapse within 3 months. In 2 cases the follow-up was inadequate and in one progress was not observed after treatment. There was immediate improvement in 2 cases, but in one of these the follow-up period was only 26 days and in the other cystitis developed, for which antibiotics were administered. Of the 9 cases in which treatment was considered to be successful, 5 were of mild urethritis [which, of course, has a tendency to clear without treatment].

The author concludes that " no strong curative claims may yet be advanced for local furacin therapy ". [This is not surprising, since the results of the trial as described are not impressive.] *Leslie Watt*

Tropical Medicine

557. **Anaemias of the Tropics, India and Ceylon**
H. Foy, A. Kondi, and B. Sarma. *Journal of Tropical Medicine and Hygiene* [*J. trop. Med. Hyg.*] **61**, 27–47, Feb., 1958. 1 fig., bibliography.

The commonest anaemia in the tropics and subtropics is of the iron-deficiency type, particularly in the hot, damp, low-lying areas, the megaloblastic type being commoner in higher and cooler regions. In the present paper the incidence and characteristics of the anaemia found in the valleys of the Brahmaputra and Surma rivers in north-east Assam, as assessed by means of a haemoglobin survey of 4,090 persons aged 15 to 40 living in the rural areas, are reported. The mean haemoglobin level was 11·5 g. per 100 ml., and in 14% of cases the level was below 8 g. per 100 ml.

Of 96 anaemic subjects selected for further investigation, 14 (15%) had megaloblastic and 82 (85%) iron-deficiency anaemia. In the former group the mean haemoglobin level was 3·7 g. per 100 ml., and these patients responded to treatment with vitamin B_{12} (cyanocobalamin) or folic acid. Most of them also had an underlying iron deficiency and required additional iron for complete cure. Few had enlargement of the liver, and no consistent abnormality was found in the serum protein pattern. In the group with iron-deficiency anaemia the mean haemoglobin level was 4·9 g. per 100 ml. The majority of these patients (89%) were women, 75% of whom were pregnant or lactating, 71% of these being below 19 years old, at which age expansion of the blood volume is still occurring. There is no deficiency of iron in the average tropical diet, but its type and composition probably reduce absorption, while the dermal loss of iron is increased in a hot climate. It is considered that while hookworm infestation may play a part in the causation of iron-deficiency anaemia, it is probably not a paramount one. *R. R. Willcox*

558. **Localized Leishmaniasis of Lymph Nodes**
D. W. Bell, J. A. G. Carmichael, R. S. Williams, R. L. Holman, and P. D. Stewart. *British Medical Journal* [*Brit. med. J.*] **1**, 740–743, March 29, 1958. 5 figs., 11 refs.

The occurrence of leishmaniasis localized to the lymph nodes in 4 British soldiers serving in Malta and Cyprus is reported. The patients complained of enlargement and tenderness of the lymph nodes in the neck, axillae, or groins; no other symptoms were present and there was no splenomegaly or hepatomegaly. Lymph-node biopsy was carried out, and in 3 of the cases Leishman–Donovan bodies were found.

The histological appearances of the biopsy tissue were similar in all 4 cases, the main features being aggregations of macrophages associated with a varying number of giant cells and, in 2 cases, severe involvement of the capsule and periadenoid tissue. Other features varied from a few scattered foci of macrophages with occasional giant cells to almost complete replacement of the normal structure by the granulomatous process. The parasites could be detected only after careful search of many sections, and were generally found near the periphery of the lymph node. Culture of aspirated lymph-node fluid in Novy, MacNeal, and Nicolle's medium was attempted, but was unsuccessful. Administration of sodium stibogluconate (" pentostam ") resulted in reduction in the size of the lymph nodes in all cases. It is pointed out that this condition should be borne in mind in the differential diagnosis of lymphadenopathy in patients from areas of endemic leishmaniasis. *I. M. Rollo*

559. **Forecasting and Control of Cholera Epidemics in South-east Asia and China**
L. Rogers. *Lancet* [*Lancet*] **1**, 151–154, Jan. 18, 1958. 2 figs., 10 refs.

The extensive endemic area of Lower Bengal is considered to be the home of cholera in Asia, although other endemic foci exist in that continent. The extension of the disease eastwards in the epidemics of 1902, 1906–9, 1918–20, 1924–6, 1932, and 1940–7 is considered in detail, and a significant correlation between the incidence of cholera and a deficient annual rainfall is noted. The author points out that the ultimate control of cholera will depend on the provision of safe drinking water in the million or more small villages in India and in the still larger number in South-East Asia and China—a task which will take decades or even centuries to perform.

In the meantime compulsory, large-scale, preventive inoculation, such as has already succeeded in India, is regarded as an urgent, immediately practicable, proceeding. In India there has been an unprecedented, rapid decline in the incidence of cholera following the adoption of the author's suggestion to inoculate compulsorily the 20 million (or so) pilgrims who were shown to play a predominating part in disseminating the disease over India and who were responsible in the nineteenth century for occasional pandemics in the Middle East and Europe. Between 1941 and 1945 about 300 million persons were inoculated in India, with the result that there has been a 40- to 50-fold reduction in the incidence of cholera in the more extensive epidemic areas. The success of these measures has led the author to extend his epidemiological inquiries to South-east Asia. In Burma alone some 300,000 labourers travel yearly to lower Burma and Eastern Bengal and are known to have spread cholera during the spring rise in incidence of the disease. In addition, some 280,000 pilgrims attend religious festivals at the Burmese pagodas. It is recommended that all pilgrims and other migrants should be compulsorily inoculated, and that those entering China from the endemic areas to the south should be inoculated at least one week before they are allowed into Chinese territory, preferably before embarking on their journey. The relation between the incidence of cholera and prevailing meteorological conditions, particularly the absolute humidity, is discussed. *R. R. Willcox*

Nutrition and Metabolism

560. **The Differential Diagnosis of Intestinal Malabsorption with I^{131}-fat and Fatty Acid**
B. J. Duffy and D. A. Turner. *Annals of Internal Medicine* [*Ann. intern. Med.*] **48**, 1–7, Jan., 1958. 7 figs., 4 refs.

Absence or deficiency of pancreatic lipase may be recognized by comparing the radioactivity of the serum lipids following the oral administration of triolein labelled with radioactive iodine (^{131}I) with that following the administration of oleic acid similarly labelled, the dose recommended in each case being 50 μc. In normal subjects and patients with non-pancreatic steatorrhoea (resulting from such conditions as Crohn's disease or following intestinal resection) the ingestion of the two substances gives rise to the same amount of serum lipid radioactivity. In patients with chronic pancreatitis or carcinoma of the pancreas, however, labelled triolein is absorbed poorly, whereas the absorption of labelled oleic acid is only a little less than in normal subjects, this difference being reflected in the respective amounts of radioactivity found in the serum lipids after their ingestion. *M. Lubran*

561. **Malabsorption Syndrome: Intestinal Absorption of Vitamin B_{12}**
S. Oxenhorn, S. Estren, L. R. Wasserman, and D. Adlersberg. *Annals of Internal Medicine* [*Ann. intern. Med.*] **48**, 30–38, Jan., 1958. 1 fig., 29 refs.

At the Mount Sinai Hospital, New York, the absorption of vitamin B_{12} (cyanocobalamin) was studied in patients with steatorrhoea by means of a modified Schilling test, the oral dose of radioactive vitamin B_{12} being 0·4 to 0·5 μg. Of 25 patients with idiopathic steatorrhoea, many in clinical and haematological remission following treatment, absorption was impaired in 20, while a low normal value was obtained in 4 and a normal value in one. There was no improvement when the test was repeated with the addition of intrinsic factor. Similar results were obtained in 3 patients with steatorrhoea following small-bowel resection. Impaired absorption of vitamin B_{12}, not improved by the oral administration of intrinsic factor, was found in 3 patients with a blind-loop syndrome. In 2 of these cases absorption was improved (but not restored to the normal level) by 2 weeks' treatment with chlortetracycline.
M. Lubran

562. **Jejunal Biopsies in Sprue**
C. E. Butterworth and E. Perez-Santiago. *Annals of Internal Medicine* [*Ann. intern. Med.*] **48**, 8–29, Jan., 1958. 8 figs., 33 refs.

In this paper from the U.S. Army Tropical Research Medical Laboratory, San Juan, Puerto Rico, are described the histological findings in jejunal biopsies obtained during laparotomy (performed for other reasons) from 15 control subjects without chronic diarrhoea and with normal intestinal absorption and from 6 patients with sprue. All 6 showed defective absorption of xylose and vitamin A, and also, to judge from the opacity of the serum after giving a test meal containing butter, of fat. In 4 cases a 12-day study of fat balance was carried out, confirming the presence of steatorrhoea.

In the normal subjects the villi were slender, projecting towards the lumen for more than half the thickness of the mucosa, and contained scattered lymphocytes, eosinophil and neutrophil granulocytes, and plasma cells, some fibrous tissue, capillaries, and lymphatics. Thick or "doubled" villi were fewer than one per low-power field. In the patients with sprue the most prominent changes consisted in oedema and inflammation of the villi and lamina propria. Many villi were short and clubbed, and fusion of villi was common. The columnar epithelium showed an excess of goblet cells. The submucosa was essentially normal. There were no "foam" cells such as are seen in Whipple's disease.

The authors consider that this histological picture could be produced by faulty epithelial regeneration, with either diminished production or shortened survival of the columnar cells. *M. Lubran*

563. **The Aetiology of Primary Hyperoxaluria**
H. E. Archer, A. E. Dormer, E. F. Scowen, and R. W. E. Watts. *British Medical Journal* [*Brit. med. J.*] **1**, 175–181, Jan. 25, 1958. 7 figs., 39 refs.

The literature on hyperoxaluria is reviewed and experimental studies designed to determine the cause of the high oxalate excretion in 2 patients (a man aged 22 years and a girl of 11) are described. Both patients had a history of recurrent oxalate stone formation and were continuously excreting in the urine abnormal quantities of oxalate (100 to 300 mg. a day). Oral administration of sodium oxalate resulted in an increase in oxalate excretion which was, however, no higher than that previously observed in controls (about 2% to 5% of the administered dose). When sodium benzoate was administered in doses of the order of 5 to 30 g. a day there was a significant depression in the amount of oxalate excreted, although no obvious effect could be detected in controls.

It is suggested that the oxalate in the urine may be derived from glycine via a pathway in which glyoxalate is an intermediate. Since sodium benzoate is excreted as a glycine conjugate (hippuric acid) it will deplete the free glycine metabolic pool and may in this way restrict excretion of oxalate. *H. Harris*

564. **Absorption of Iron as a Problem in Human Physiology. A Critical Review**
H. W. Josephs. *Blood* [*Blood*] **13**, 1–54, Jan., 1958. 6 figs., bibliography.

Gastroenterology

565. **Further Observations on the Use of I^{131}-labeled Lipids in the Study of Disease of the Gastrointestinal Tract**

J. M. RUFFIN, I. C. KEEVER, C. CHEARS, W. W. SHINGLETON, G. J. BAYLIN, J. K. ISLEY, and A. P. SANDERS. *Gastroenterology* [*Gastroenterology*] **34**, 484–490, March, 1958. 8 refs.

In previous papers from Duke University School of Medicine, Durham, N. Carolina, the authors have drawn attention to the usefulness of lipids labelled with radioactive iodine (^{131}I) in the study of gastro-intestinal diseases (see *New Engl. J. Med.*, 1956, **255**, 594; *Abstr. Wld Med.*, 1957, **21**, 170). In the present paper the results of tests on 556 patients with labelled triolein and on 46 patients with both labelled triolein and labelled oleic acid are analysed. The 556 patients were classified in four groups: 216 had undergone operations for peptic ulcer, 39 had diseases of the pancreas, 31 had diseases of the small intestine, and 250 belonged to a miscellaneous group which included cases of functional gastro-intestinal disorders, ulcerative colitis, duodenal ulcer, diabetes, cirrhosis of the liver, and other conditions. The 46 patients on whom the double test was performed included 35 who had undergone gastric resection, 6 with pancreatic disease, 3 with sprue, and 2 with regional enteritis.

Of the patients who had undergone gastrectomy or gastro-enterostomy, with or without vagotomy, absorption of triolein was impaired in about 60%, suggesting that malnutrition following such operations may be secondary to faulty absorption or digestion of fats. The fact that oleic acid absorption was normal in those patients in this group in whom it was tested tends to indicate that the fault lies rather in digestion than in absorption. The results obtained in the other categories showed that impairment of absorption of both triolein and oleic acid indicates a disease of the small bowel, while impairment of absorption of triolein with normal absorption of oleic acid is strongly suggestive of pancreatic disease. In all patients in the miscellaneous group the absorption of triolein was normal.

The authors consider that these tests provide a simple, reliable, and accurate procedure for the measurement of fat absorption. *Z. A. Leitner*

566. **Cardiomyotomy for Achalasia of the Cardia. The Experience of the Middlesex and Harefield Hospitals up to 1955**

E. D. ACHESON and G. D. HADLEY. *British Medical Journal* [*Brit. med. J.*] **1**, 549–553, March 8, 1958. 3 figs., 16 refs.

Between 1947 and 1955 cardiomyotomy was performed for achalasia of the cardia on 26 patients at the Middlesex Hospital, London, and 9 at Harefield Hospital, Middlesex, and in this paper the results are assessed. There were 8 males and 27 females, and the average age at the time of operation was 45 years. Symptoms had been present for an average of 10 years. The majority of the patients had received treatment previously. In 14 there was a history of respiratory infection and in 4 there was evidence of rheumatoid arthritis.

The technique consisted in a single longitudinal incision in the oesophagus down to the submucosa. No correlation was found between the length of the incision and the clinical success of the operation. There were no operative deaths; 2 patients died subsequently from coronary thrombosis and 2 were untraced. Complete follow-up information was available concerning 27 of patients. In 7 the operation failed, further treatment being required for dysphagia. Only one patient was considered to be cured, but 19 were improved. (The patients themselves assessed the results more favourably.) Regurgitation was usually effectively relieved, but dysphagia was less so. Many patients suffered after the operation from heartburn, which was presumed to be due to reflux of gastric juice, but few of them considered this to be a very important disability. In one patient anaemia developed and in another a fibrous stricture. Most of the patients showed gain in weight. Radiological improvement, which was noted in just over half the cases, occurred most often in those with a short history or those in which the radiological changes before operation were not severe.

The authors conclude that when surgery is indicated cardiomyotomy " in spite of its manifest imperfections remains the best available surgical operation for achalasia of the cardia ". *M. Meredith Brown*

567. **Clinical Studies of Porphyrinuria in Liver Diseases.** (Klinische Untersuchungen über Porphyrinurie bei Leber-erkrankungen)

R. KEHL. *Zeitschrift für klinische Medizin* [*Z. klin. Med.*] **155**, 1–24, 1958. Bibliography.

At the University of Marburg, Germany, the author has carried out quantitative and qualitative studies on the urinary excretion of porphyrins in 66 patients with various types of liver damage. An increased excretion of coproporphyrin in the urine was found to be a sensitive index of hepatic parenchymal damage, and in patients with hepatitis urinary excretion values returned towards normal during recovery. However, the correlation with the degree of liver damage as assessed by histological and other methods was not high, though raised coproporphyrin excretion was often associated with a raised plasma γ-globulin content. It is pointed out that since coproporphyrin excretion in the urine is also increased in obstructive jaundice the estimation is of little value in the differential diagnosis of jaundice. In patients with progressive cirrhosis, coproporphyrin excretion was increased, but values within normal limits

were often found in patients with well compensated hepatic cirrhosis.

Detailed results for each of the 66 patients are presented in a 13-page table. *P. C. Reynell*

MOUTH AND TONGUE

568. **Lichen Planus of the Mouth**
R. P. WARIN, H. S. M. CRABB, and A. I. DARLING. *British Medical Journal* [*Brit. med. J.*] **1**, 983–984, April 25, 1958. 13 refs.

Lesions of the oral mucous membrane are present in over 50% of cases of cutaneous lichen planus, but such lesions with minimal or without cutaneous lesions are much less frequently seen. In this paper the findings in 45 cases of lichen planus of the mouth with minimal or no cutaneous eruption seen at the United Bristol Hospitals during the period 1950–7 are summarized.

The lesions consist of discrete or confluent white spots of pinhead size, white streaks, or, less commonly, white patches. Females are affected twice as often as males, and most of the patients are in the 5th and 6th decades. There may be no symptoms, but more often there is intermittent pain or roughness or dryness of the mouth. There does not appear to be any association with smoking. In about half the cases there is a history of a nervous breakdown, insomnia, or depression, and most patients appear to be of a nervous, sensitive temperament. The site most commonly affected is the inner aspect of the cheek, and then the tongue, the lips, the gum margins, and the palate and fauces. Ulceration occurs at times in most cases. The condition tends to be of long standing, and in one case (and possibly a second) in the authors' series carcinoma supervened on pre-existing ulcerative lesions.

The differential diagnosis is briefly considered.
R. B. Lucas

569. **Treatment of Aphthous Ulceration of the Mouth**
S. C. TRUELOVE and R. M. MORRIS-OWEN. *British Medical Journal* [*Brit. med. J.*] **1**, 603–607, March 15, 1958. 1 fig., 16 refs.

The authors, writing from the Radcliffe Infirmary, Oxford, review the various theories regarding the aetiology of aphthous ulceration of the mouth and describe its main features, pointing out that there are two types, the common minor form and the major form, in which the ulcers are deep and chronic and produce a severe degree of illness. The reported findings on the use of cortisone and its analogues in the treatment of this disorder are next briefly reviewed. The variable results obtained by different workers may, it is suggested, be attributable to the use of an ointment as the vehicle for carrying hydrocortisone to the lesions in the mouth, a method which is far from suitable for this type of local therapy.

They then report the results of a clinical trial of the hemisuccinate sodium salt of hydrocortisone given in the form of a tablet with a lactose base which on dissolving in the mouth produces a solution of hemisuccinate to bathe the lesion. In 23 cases of the minor form of the complaint a tablet was applied locally as soon as an ulcer appeared. The tablet took about three-quarters of an hour to dissolve, and the pain of the ulcer was usually relieved by the time this had happened. One tablet was applied in this way up to four times a day until the ulcer disappeared, which it usually did in 36 to 48 hours. It was noted that if this treatment was applied early to small ulcers they did not develop into the usual full-sized lesion. All except one of the 23 cases responded to this method of treatment; the authors describe 3 typical cases.

In the 22 cases of the major form a similar method was adopted, one tablet being given four times a day and this regimen continued until ulceration had ceased. Initially all patients made a good response. Subsequently maintenance treatment was carried out in which most patients received 2 tablets a day and a few the full dose of 4 tablets. On such treatment 5 patients remained completely free for several months, and most of the others, while still continuing to get occasional minor lesions, never developed actual ulceration and the severe disability previously suffered was reduced to negligible proportions. The same tablets were employed in the treatment of Behçet's syndrome, the Stevens–Johnson syndrome, and in aphthous ulceration occurring in association with idiopathic steatorrhoea and ulcerative colitis. In all these conditions there was an extremely satisfactory response to this method of treatment.
T. D. Kellock

STOMACH AND DUODENUM

570. **The Secretor Status in Duodenal Ulcer**
J. WALLACE, D. A. P. BROWN, I. A. COOK, and A. G. MELROSE. *Scottish Medical Journal* [*Scot. med. J.*] **3**, 105–109, March, 1958. 16 refs.

Since Aird *et al.* (*Brit. med. J.*, 1954, **2**, 315; *Abstr. Wld Med.*, 1954, **16**, 464) demonstrated a significantly increased incidence of Group-O blood among patients with peptic ulcer, other workers at several centres have been studying the mechanism of this association, with special reference to secretor status. This work has shown that some individuals secrete certain blood group substances (ABH) of a mucopolysaccharide nature into the saliva and gastric juice, while others do not. Aird *et al.* suggested that the presence of these blood group substances in the secretions might help to afford protection against peptic ulceration.

In a study reported from the Western Infirmary and Blood Transfusion Service, Glasgow, the secretor status of 415 patients with peptic ulcer has been determined. In 214 of these patients who had blood of Group A, B, or AB the saliva was compared with that of 242 suitable control subjects of similar blood group; while in the remaining 201 patients who were of Group O and 261 random Group-O blood donors the Lewis blood groups were compared, for it has been established that virtually all Le^a-positive individuals are non-secretors of H substance, though approximately 7% of Le^a-negative persons are also non-secretors. (The figures for this second group

of subjects are therefore approximate, and a further study using a potent anti-H substance is planned.) It was found that in both groups there was a significantly greater proportion of non-secretors of blood group substances among patients with peptic ulcer ($P<0{\cdot}01$). In patients with duodenal ulcer the severity of ulceration appeared to influence the secretor status. Thus among patients in whom ulcer was diagnosed by radiography only there was no significant increase in the number of non-secretors over the control group, but among those with ulcers severe enough to require surgical treatment there was such an increase. The numbers of patients with gastric ulcer, combined gastric and duodenal ulcer, and stomal ulcer were too small to provide conclusive information.

The authors come to the conclusion that the mucopolysaccharides which contain the blood group substances protect the mucosa against peptic ulceration. They also suggest that the secretor status may be of prognostic value in peptic ulcer, and that the absence of blood group substances may be an additional indication for surgical treatment.

[This is an important contribution to the subject.]

B. F. Swynnerton

571. **The Effect of a Prolonged Acting Form of Propantheline Bromide (Pro-banthine) on Hydrogen Ion Concentration of Gastric Juice as Observed in Forty-eight-hour Gastric Analysis**

A. M. KASICH and T. G. ARGYROS. *Gastroenterology* [*Gastroenterology*] **34**, 232–238, Feb., 1958. 2 figs., 5 refs.

The effect on the acidity of the gastric secretion of a prolonged-acting form of propantheline (" pro-banthine ") has been studied in 32 cases of peptic ulcer at the Lenox Hill Hospital, New York. After passing a stomach tube the *p*H of the gastric juice was determined on 5-ml. samples taken at intervals of one to 2 hours, first during a 24-hour control period and then after the administration of 2 doses of propantheline given 12 hours apart, 16 patients receiving 30 mg., 8 patients 60 mg., and 8 patients 120 mg. in each dose.

There was a slight decrease in acidity as compared with the control period in 56% of the patients given 30-mg. doses, and a considerable decline in patients given the 60-mg. and 120-mg. doses, the *p*H remaining at about 4 during both day and night. Since side-effects, such as dryness of the mouth, were not severe with doses of 60 mg. twice a day, this is recommended as the optimal therapeutic dose of propantheline in the control of gastric acidity.

Kenneth Gurling

572. **Effect of Smoking on the Production and Maintenance of Gastric and Duodenal Ulcers**

R. DOLL, F. AVERY JONES, and F. PYGOTT. *Lancet* [*Lancet*] **1**, 657–662, March 29, 1958. 14 refs.

A detailed statistical study is reported of the relationship between smoking and the development and maintenance of peptic ulcer. As the authors state, " the results of the inquiry into patients' smoking habits are difficult to interpret ". [Important questions, such as whether smoking causes ulcer or ulcer causes smoking or whether both are due to a common cause, still remain unanswered.] The only clear facts that emerged from this investigation were the following: (1) There were fewer non-smokers among patients with gastric ulcer of both sexes and among male patients with duodenal ulcer than among controls. (2) The proportion of smokers who smoked only cigarettes was higher in patients with gastric ulcer than in the control group, but [surprisingly] the proportion smoking both pipes and cigarettes was significantly lower. There were no significant differences in this respect between the patients with duodenal ulcer and controls. (3) The rate of healing of gastric ulcer was more rapid in patients who were advised to stop smoking than in those who were not so advised. The average degree of healing in patients who were not smoking on admission was practically the same as that in patients who continued to smoke.

R. Schneider

573. **Physiologic, Psychologic, and Social Determinants in the Etiology of Duodenal Ulcer.** [Review Article]

I. A. MIRSKY. *American Journal of Digestive Diseases* [*Amer. J. dig. Dis.*] **3**, 285–314, April, 1958. 14 figs., bibliography.

574. **Recurrence of Hemorrhage from Medically Treated Gastric Ulcers. Four- to Eight-year Follow-up of Forty-seven Patients**

I. M. ARIAS, N. ZAMCHECK, and W. B. THROWER. *A.M.A. Archives of Internal Medicine* [*A.M.A. Arch. intern. Med.*] **101**, 369–376, Feb., 1958. 13 refs.

In this paper from the Boston City Hospital the authors report their findings at follow-up examination of 47 patients who had had haemorrhage from a proven gastric ulcer and had been treated medically.

Over a period of 4 years 119 patients were admitted to the hospital because of gastro-intestinal haemorrhage, and in all of them one or more gastric ulcers were found on *x*-ray examination or at gastroscopy. A total of 69 patients were excluded from the study—49 who were operated on, 9 in whom there was haemorrhage from causes other than or in addition to a gastric ulcer, and 11 who died during the initial period of medical treatment. Of the remaining 50 patients (31 males and 19 females), 18 were over 65 years of age, and in 37 there was a history of gastric ulcer for at least one year. Adequate follow-up information was available in respect of 47 of these for periods ranging from 4 to 8 years after the initial medical treatment. Haemorrhage recurred in only 3 cases, and other complications, such as perforation or pyloric stenosis, occurred in 6. There were no cases of gastric carcinoma. Symptoms of gastric ulcer, however, recurred in 30 cases. Of the 9 patients who were considered to require surgical treatment but who refused it, only one had a further haemorrhage; all survived.

The view that the risk of recurrent haemorrhage from a benign gastric ulcer makes surgery necessary is not, in the authors' judgement, supported by these findings, even in older patients. It is pointed out, however, that im-

mediate radiological or gastroscopic examination is essential for the satisfactory diagnosis of many gastric ulcers which would otherwise not be detected.

J. Warwick Buckler

575. **Long-term Results of Vagotomy and Gastro-enterostomy in Chronic Duodenal Ulceration. A Comparison with Gastrectomy**

H. BURGE and E. J. PICK. *British Medical Journal* [*Brit. med. J.*] **1**, 613–615, March 15, 1958. 9 refs.

The authors report, from West London Hospital Medical School, the results of an investigation into the long-term results of vagotomy and gastro-enterostomy in the treatment of chronic duodenal ulceration. Of 301 patients so treated at various surgical centres in Great Britain finally available for review, only 6 were untraced and 13 had died of unrelated causes. For the remaining 282 cases the follow-up period ranged from 7 to 9 years and the recurrence rate, as judged by perforation, haemorrhage, or need for further operation, was 4·25%.

The review was made by questionary or interview. Nutritional status was good, 14% having gained weight, 75% having maintained their weight, and only 11% having lost weight. The incidence of anaemia in a group of 50 unselected cases 8 years after operation was investigated, and in only one case was the haemoglobin level found to be below 85%. On the other hand direct questioning elicited that 30% of the patients suffered from diarrhoea or loose motions, but in no case was it severe enough to cause the patient to seek medical advice. Typically, it consisted in bouts lasting from one to 3 days at a time, in which three to four loose stools were passed each day; these attacks came on at intervals of one to 3 months. Mild post-cibal symptoms were reported in 16% of cases, but there was no case of severe "dumping". Bilious regurgitation was present in 13%.

The authors then compare these results with those found in patients treated by partial gastrectomy. They conclude that vagotomy and gastro-enterostomy carries a lower mortality rate, a similar recurrence rate (but one which, they suggest, might have been considerably lower if vagal resection had been complete in a higher proportion of cases), a better nutritional state, and particularly a considerably lower incidence of anaemia. Diarrhoea may be slightly more frequent, although interrogation of patients treated by gastrectomy revealed that about 20% of these also had this symptom. Bilious regurgitation and post-cibal symptoms were both very much less after vagotomy and gastro-enterostomy than after partial gastrectomy. *T. D. Kellock*

576. **Method of Testing for Complete Nerve Section during Vagotomy**

H. BURGE and J. R. VANE. *British Medical Journal* [*Brit. med. J.*] **1**, 615–618, March 15, 1958. 6 figs., 8 refs.

The authors point out that incomplete nerve section during the operation of vagotomy for peptic ulcer is frequently followed in a few months by complete recovery of function. They describe a method for determining the completeness of vagal section which can be carried out during the course of the operation and which should be of great benefit in lowering the incidence of recurrent ulceration, since it enables the surgeon to search for and divide smaller branches of the vagi which may have been overlooked.

The method, which consists in the application of a simple physiological technique whereby the rise in intragastric pressure due to contraction of the stomach on stimulation of the vagi is recorded, was first validated in cats. It is described as follows. A large-bore cuffed tube is passed through the mouth until the tip is in the stomach; a special encircling electrode is applied to the lower end of the oesophagus and the cuff inflated, thus sealing off the oesophagus and bringing the vagi into close contact with the electrode. The pyloric antrum is then occluded by a light clamp and the stomach filled with water, an amount between half and one litre giving the best result. The optimum frequency for stimulation was found to be 10 per second, and the most suitable potential difference 40 to 50 volts. After a control stimulation all the branches of the vagi that can be found are cut, and then a further stimulus is applied; if this produces no rise at all in gastric pressure it can be assumed that all the branches have been divided. If, however, a further rise does occur search must be undertaken for a small branch of the vagus that has been overlooked.

It was found in experiments on both the cat and man that a considerable rise in intragastric pressure would occur even if only a very small amount of vagal nerve tissue was left. In 16 human patients the number of nerve trunks varied from 2 to 7, and in 14 of these there were 3 or more branches. An improved electrode controlled by a rotary switch allows the stimulus to be applied to each of four quadrants in turn and so facilitates the location of any uncut branch. *T. D. Kellock*

INTESTINES

577. **Ileostomy Chemistry**

B. N. BROOKE. *Diseases of the Colon and Rectum* [*Dis. Colon Rect.*] **1**, 3–14, Jan.–Feb., 1958. 11 figs.

This study was based on the analysis of 24-hour samples of fluid taken from the ileal stoma of patients who, with one exception (a case of polyposis of the colon), had been operated on for ulcerative colitis. During the immediate postoperative period the loss of nitrogen in the ileal fluid was between 3 and 4 g. per day, but the period of negative balance lasted no longer than after ordinary operations; later the loss of nitrogen fell to 1 to 2 g. per day. The essential amino-acids glycine, alanine, valine, leucine, and arginine were all demonstrated in the fluid, but the loss was not significant since patients continued to gain weight.

The loss of nitrogen and sodium depended on the volume of ileal fluid lost, which in some cases was more than 2 litres daily in the first postoperative week, but later fell to 250 to 500 ml. daily. The sodium loss, which at first was considerable at 200 to 400 mEq. per litre with no evidence of conservation by the kidney,

later fell to about 150 mEq. per litre. This loss may lead to a salt depletion crisis in the immediate postoperative phase and to prevent this the author recommends that a prophylactic infusion of saline be given, assuming a loss of some 300 mEq. in each litre of ileal fluid. The preoperative loss of potassium in such cases is usually corrected by the performance of ileostomy; in 5 of the author's cases the loss was less than 20 mEq. per day or 10 mEq. per litre. Apparently no attempt at conservation of potassium is made by the kidney, although there may be a reciprocal relationship between the loss of sodium and potassium. In 2 patients with ileal diarrhoea or secondary ileitis a loss of 30 mEq. of potassium per litre occurred. The effect of cortisone on the levels of sodium and potassium in the ileal fluid was studied in 3 patients. Cortisone reduced the volume of the excreta from the stoma and the volume of urine. The loss of sodium in the ileal fluid fell to that seen in patients with an established stoma, although the loss in the urine was increased. The loss of calcium, which is high and does not decrease, is not of serious concern in the immediate postoperative phase, but might lead ultimately to decalcification of bone. The loss of 50 to 60 mEq. per day (or just over 1 g.) is more than the ordinary loss in the stools of normal subjects, suggesting that the colon plays some part in the absorption of calcium. The significance of the drain on calcium stores is being assessed in further studies now being undertaken. *A. Gordon Beckett*

578. **Rectal Biopsy in Ulcerative Colitis**
G. LUMB. *Diseases of the Colon and Rectum* [*Dis. Colon Rect.*] **1**, 37–43, Jan.–Feb., 1958. 3 figs., 1 ref.

This study of the morbid histology of ulcerative colitis is based on the findings in 271 biopsy specimens taken from 236 cases of the disease at the Gordon Hospital, London. Evidence of active disease was present in 170 specimens and of quiescent disease in 83. Usually the correlation between histological and sigmoidoscopic appearances was good, but in 23 cases showing normal sigmoidoscopic appearances microscopical examination revealed characteristic histological changes. In acute cases the earliest change was seen in the bases of the crypts, where an intense, acute, inflammatory process occurred, leading to abscess formation. In one-third of these cases excessive infiltration by eosinophil granulocytes was present. Ultimately the crypt walls break down and ulcers develop; these are rarely clear-cut, and present an irregular pattern of necrotic debris scattered among fragments of viable epithelium. Sometimes the inflammatory process spreads into the submucosa and causes the shedding of strips of overlying mucosa. Submucosal involvement occurred in 9 of the active cases and in 36 of the total series, these being usually cases of long standing. It was observed that the mucosa became oedematous, with many dilated and congested capillaries, and in some cases there was bleeding into ruptured crypts. Increased numbers of goblet cells were present in the surrounding epithelium, these producing mucus which coated the adjacent mucosa.

In mild cases the processes of damage and repair tended to go on together. In the quiescent cases the intact mucosa had a considerably altered structural pattern, showing diminution in the number of crypts, generalized thinning, and more goblet cells than usual. During healing dense accumulations of lymphocytes were present below the epithelium, lymphoid follicles became apparent (equivalent to the granularity seen on sigmoidoscopy), and eosinophilic mucinous material spread over the irregular surface. The lymphocytes disappeared, leaving dilated lymph channels. The muscularis mucosae was often separated from the mucosa by a wide zone of oedematous connective tissue with a considerable number of young fibroblasts and capillaries and, later, fibrous tissue. An ulcerated area sometimes healed and was obliterated by fibrous tissue drawing together adjacent areas of mucosa. The state of quiescence, as judged by biopsy appearances, gave no indication of the subsequent course of the disease.

From a further study of the early lesion in minute foci of disease in colectomy specimens the author concludes that the earliest abnormality is a minute erosion in the crypts of Lieberkühn, usually at the base and isolated from other similar lesions. There was no evidence of primary vascular disease or of previous abnormality of the basement membrane. The most severe lesions, in which perforation and dilatation of the colon were most likely to occur, were in areas of freshly involved mucous membrane. For this reason the author suggests that it is probably unwise to attempt to save any of the colon once the decision to operate has been made.

A. Gordon Beckett

579. **Steroid Hormones in the Management of Chronic Ulcerative Colitis. Indications and Contraindications**
E. D. KIEFER. *Diseases of the Colon and Rectum* [*Dis. Colon Rect.*] **1**, 15–22, Jan.–Feb., 1958. 18 refs.

In a review of 100 cases of ulcerative colitis treated with steroid hormones at the Lahey Clinic, Boston, the author reports than in 70 of these there was an excellent and in 11 a fair immediate response, while 19 patients derived no benefit. Almost all those without serious secondary infection or organic disease (29 out of 31) responded well, whereas of those with sepsis, less than two-thirds improved, the majority of those improving being without serious organic change. In those with serious organic change indicating long-standing disease the bowel symptoms persisted virtually unchanged. Prolonged remission occurred in 70% of the non-infected group and 44% of the infected group, almost all these being cases without serious organic change. In this series there was no case of perforation of the colon or suppression of adrenal function, but gross intestinal haemorrhage during steroid therapy occurred in 3 cases.

The author concludes that the corticosteroids should be used early in the treatment of ulcerative colitis, when there is little or no infection and no fibrosis. He found little difference between the various steroids available. Prednisone has the advantage that it can be given by mouth and has less tendency to upset the fluid and electrolyte balance, but its continuous use seems inadvisable in the present state of our knowledge.

A. Gordon Beckett

Cardiovascular System

580. **Blood Pressure in White People over 65 Years of Age**

A. M. MASTER, R. P. LASSER, and H. L. JAFFE. *Annals of Internal Medicine* [*Ann. intern. Med.*] **48**, 284–299, Feb., 1958. 3 figs., 36 refs.

Since the number of elderly persons in the population is increasing, the establishment of normal limits of blood pressure in the aged becomes more important. The casual sitting blood pressure of 5,757 white U.S.A. subjects aged 65 to 106 years was recorded in the study here reported from the Mount Sinai Hospital, New York. These 2,998 men and 2,759 women were selected as being all apparently healthy, ambulant, living in the community, and completely able to take care of themselves; none had cardiovascular disease. The systolic pressure was recorded at the beginning of Korotkoff's sound and the diastolic at its complete disappearance.

The findings, which were analysed statistically, showed that after the age of 65 the blood pressure does not consistently rise with increasing age as it does before that age. In both sexes the mean systolic pressure rises slightly until age 70 to 74; thereafter it remains at a mean of 145 mm. Hg in men, but in women it declines from a mean of 159 mm. at age 74 to a mean of 149 mm. Hg at age 95. In both sexes the diastolic pressure is practically constant after age 65, the mean being 83 mm. Hg in men and 85 mm. Hg in women. The mean blood pressure for all the men in this study was 145/82 mm. Hg, and for the women 156/84 mm. Hg, the mode being 140/80 mm. Hg for both sexes. The pulse pressure was larger in women at all ages. Two sets of "normal" limits of blood pressure for each age group were calculated. The "middle 80% range" (that is, all readings within $\pm 1{\cdot}282\sigma$ of the mean) was 115/70 to 175/95 mm. Hg for men and 120/65 to 192/102 mm. Hg for women. The "middle 95% range" ($\pm 2\sigma$) was 100/62 to 190/102 mm. in men and 100/55 to 212/112 mm. in women. The authors state that a blood-pressure reading beyond these limits is practically always abnormal, but emphasize, of course, that in individual patients all clinical aspects must be considered when assessing the significance of such readings. *D. Emslie-Smith*

581. **Relationship of the Blood Pressure to Weight, Height and Body Build in Apparently Healthy Subjects, 65–106 Years of Age**

A. M. MASTER and R. P. LASSER. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **235**, 278–289, March, 1958. 1 fig., bibliography.

The relationship between blood pressure and height, weight, and body build in apparently healthy subjects over 65 years of age was studied at Mount Sinai Hospital, New York, in the replies to questionaries obtained from all parts of the U.S.A. After exclusion of subjects who lived in institutions and those who had symptoms of cardiovascular disease there remained 5,612 (2,922 males and 2,690 females), aged 65 to 106, for whom information was available. Each sex was divided into 5-year age groups from 65 to 89 years, subjects 90 and over being grouped together. The subjects in each age group were then classified for height as short, average, or tall according to insurance company standards, and for weight as underweight, average, moderately overweight, and severely overweight compared with the average for height. For each of these categories the average blood pressure was estimated, and it was found that "as a general rule, the mean systolic and diastolic pressures increase with increasing weight". Since it has been shown that the average blood pressure undergoes little change after the age of 65 [see Abstract 580], all the subjects were grouped according to height and weight and the blood-pressure values studied. The mean blood pressure of the average-weight males was 145/82 mm. Hg and of average-weight females 157/85 mm. Hg. Height did not appear to be closely related to blood pressure, nor did absolute weight, but rather the deviation from the average weight for a given height. Blood-pressure readings were lowest in underweight males in each height group (141/78, 139/79, 139/79 mm. Hg, respectively) and highest in severely overweight males (151/85, 159/85, 153/87 mm. Hg, respectively). A similar trend, although the actual readings were higher, was seen in females, but in short females the average systolic pressure in all except the underweight was 157 mm. Hg. Since this series of subjects was highly selected it is suggested that the effect of obesity upon blood pressure may be minimized. The reasons for higher blood pressure in the obese and the clinical significance of the variations with body build are discussed.

[Howell in 1942 showed that in a group of Chelsea Pensioners aged 65 to 100 there was a rise in blood pressure with age, the peak being reached in the age group 75 to 79 (166/87 mm. Hg), followed by a decline in the older groups.] *V. Reade*

582. **Respiratory Viruses and Heart Disease**

E. N. SILBER. *Annals of Internal Medicine* [*Ann. intern. Med.*] **48**, 228–241, Feb., 1958. Bibliography.

During 1950–6 complement-fixation tests for viruses and rickettsiae and cold haemagglutinin tests were performed on acute and convalescent sera of patients admitted to the Michael Reese Hospital, Chicago, with the following features: (1) congestive cardiac failure without evident cause; (2) heart disease developing during or after an acute infectious illness which was either definitely viral or at least not of bacterial or rheumatic aetiology; (3) electrocardiographic evidence suggestive of myocarditis. A fourfold or greater rise of specific antibodies for a particular virus during the course of the illness was regarded as diagnostic. In 23 cases the heart

disease was presumed to have been caused by respiratory viruses, a specific viral cause being actually identified in 8 cases. There were 2 cases of subacute pericarditis, both caused by the virus of influenza B. Of the 15 cases of acute myocarditis, 4 were due to influenza A, influenza A′, psittacosis, and primary atypical pneumonia viruses respectively, the other 11 cases being presumptive. Of the 3 cases of subacute myocarditis, one was infected with both influenza A and B viruses. Of the 3 cases of chronic myocarditis, one was caused by influenza B virus and was fatal.

The author reviews the literature of viral heart disease and of certain cardiomyopathies of unknown aetiology. He concludes that respiratory viruses are a cause of both acute and chronic heart disease and suggests that cases of Fiedler's myocarditis, benign idiopathic pericarditis, post-partum heart disease, and endocardial fibroelastosis may be caused by myocardial involvement by viruses. If the latent period between the upper respiratory infection and the onset of heart disease is not borne in mind the cardiac complication may be wrongly regarded as a fresh disease. *D. Emslie-Smith*

583. **Reliability of Electrocardiographic Diagnosis of Left Ventricular Hypertrophy**
A. Selzer, C. L. Ebnother, P. Packard, A. O. Stone, and J. E. Quinn. *Circulation* [*Circulation*] **17**, 255–265, Feb., 1958. 20 refs.

Because the replies to a recent questionary revealed some hesitation by several authorities in accepting a strictly defined set of criteria for the electrocardiographic (ECG) diagnosis of left ventricular hypertrophy the authors, working at the Veterans Administration Hospital, San Francisco, have analysed the necropsy reports in 550 cases in which ECG records were available. Of these ECGs, 108 showed left ventricular hypertrophy uncomplicated by other (defined) factors, the diagnosis being based on increased voltage or prolonged ventricular activation time; ST–T changes were accepted only in combination with one or both of these abnormalities. The heart weight, graded as below 450 g., between 450 and 550 g., or above 550 g., was used in the anatomical diagnosis of left ventricular hypertrophy. Among the 108 cases the ECG diagnosis was confirmed pathologically in 75, was doubtful in 16, and unconfirmed in 17. Closer study of the clinical records of the 17 false positive cases showed that none of these patients died of cardiovascular disease and none had left ventricular hypertrophy, the majority having died of cancer and being emaciated.

The authors observe that the criteria for the ECG diagnosis of ventricular hypertrophy are empirical, but that theoretical considerations related to the increased mass of heart muscle could account for the changes usually described; it is noted that most of the false positive cases occurred in unusually thin subjects, which might account for magnification of a normal depolarization force. Ventricular activation time in left-sided precordial leads was abnormal in 6 of the 17 false positive cases, although it was normal in nearly half of the patients with the heaviest hearts. The authors conclude that the ECG criteria discussed cannot be claimed to confirm more than a probability that the left ventricle is hypertrophied, this probability being higher in persons of average build and lower if the chest wall is thin. The greatest errors occur in attempts to diagnose grades of hypertrophy. *R. S. Stevens*

584. **Clinical Aspects of High-grade Heart-block**
A. R. Gilchrist. *Scottish Medical Journal* [*Scot. med. J.*] 3, 53–75, Feb., 1958. 19 figs., 35 refs.

This paper is based on the author's personal experience in 140 selected cases of heart block seen at the Royal Infirmary, Edinburgh, over a period of many years. Three grades of heart block are commonly recognized: (*a*) first-degree block, with delayed conduction; (*b*) second-degree block, with dropped beats; and (*c*) complete block with dissociation of the auricular and ventricular rhythms. Second-degree block is subdivided into two types, Type I being characterized by progressive lengthening of successive P–R intervals leading to simple ventricular omissions, the A:V ratio ranging from 8:7 to 2:1, while in Type II there is an abrupt rhythmic omission of ventricular beats in regular sequence without lengthening of the P–R interval, the A:V ratio being 2:1, 3:1, or more rarely 4:1.

The author describes in detail the clinical features of each grade of heart block. The importance is stressed of differentiating 2:1 block of Types I and II because of their different prognostic significance, the induction of auricular tachycardia by exercise or intravenous injection of atropine reducing the degree of block in Type I and increasing it in Type II. Complete heart block as an acute incident is usually the result of posterior myocardial infarction and, in the author's experience, bears a better immediate prognosis than has hitherto been supposed. In none of his patients who survived the initial infarction did complete heart block become permanent. The development of chronic complete block may follow one of two courses. The essential feature of the first is a liability to recurrent syncopal attacks resulting from ventricular standstill which is followed by a short period of complete heart block; permanent complete block may not appear for some years. Alternatively, a Type-II second-degree block may progress gradually to complete block, at first intermittent and later permanent, Stokes-Adams attacks occurring less frequently than in cases of the former type. The author describes some of the features of chronic complete block, stressing the point that the heart rate may accelerate with exercise or emotion. He cites 2 cases of complete block which, after many years, reverted to sinus rhythm and gives a number of examples of high-grade block associated with either drug intoxication or a hypersensitive carotid-sinus mechanism. *Francis Page*

585. **Inaccuracy of Wedge Pressure as an Index of Pulmonary Capillary Pressure**
J. P. Murphy. *Circulation* [*Circulation*] **17**, 199–203, Feb., 1958. 9 refs.

At Creighton University School of Medicine, Omaha, Nebraska, the pulmonary capillary pressure, measured by the " wedge " technique, was compared with a direct

measurement of the left atrial pressure in 12 subjects with congenital or acquired heart disease. All the studies were performed in basal conditions under local analgesia, the left heart being entered by direct needle puncture from the right paravertebral approach (after the method of Björk) and the right heart by the standard catheterization technique; all pressures were measured by means of a strain gauge with photographic oscilloscopic recording. The site of determining the wedge pressure was that point in the pulmonary tree beyond which a No. 4 catheter would not pass, but at which fully oxygenated blood was obtained.

A good correlation between the left atrial pressure and wedge pressure was obtained in 5 of the patients in whom the left atrial pressure was within normal limits. But in 7 patients with raised left atrial pressure the wedge pressure differed from that in the left atrium by between 9 and 33 mm. Hg. The author therefore favours the use of direct left heart catheterization, particularly in cases of mitral stenosis with marked increase in left atrial pressure, since here the wedge pressure reading is especially inaccurate. *P. Hugh-Jones*

586. **A Critical Study of the Concept of Portal Hypertension.** (Étude critique du concept d'hypertension portale)

L. Léger, L. Marcenac, G. Charles, and C. Gutel. *Revue française d'études cliniques et biologiques* [*Rev. franç. Ét. clin. biol.*] **3**, 141–153, Feb., 1958. 9 figs., 12 refs.

The authors question the classic view that portal hypertension is always due to an obstructive lesion in the liver or the portal venous system. In 6 patients with portal hypertension studied at the Hôpital Lariboisière, Paris, the intrasplenic pressure was measured before and shortly after the performance of porta-caval anastomosis. Although the pressure fell after operation in all cases, in none did it reach the normal level. In 2 other cases they found that the intrasplenic pressure was raised in spite of an extensive "spontaneous" collateral circulation. They quote examples of the syndrome of obstruction of the splenic vein, usually due to pancreatic disease, and mention a case in which there was also a raised pressure in a patent portal vein. Finally, they give a description of 2 patients with oesophageal varices in whom the intrasplenic pressure did not rise after ligation of the varices as it would be expected to do according to the classic view.

They consider that these findings are best explained by assuming that portal hypertension is partly due to an increased inflow of blood into the portal system through (hypothetical) arterio-venous anastomoses in the spleen or small intestine. They have carried out mesenteric arteriography on dogs and claim to have demonstrated rings of active constriction at the bifurcations of the small arteries which they suggest may regulate the inflow of blood into the portal vein.

[The abstracter finds these arguments unconvincing and has grave doubts about the accuracy of the authors' pressure recordings. Neither their technique nor the point of reference above which they measured the intrasplenic pressures is specified, and some of the readings which they quote are considerably higher than those found in similar cases by other workers.] *P. C. Reynell*

CONGENITAL HEART DISEASE

587. **Severe Valvular Pulmonary Stenosis with Normal Aortic Root. Immediate Results of Transarterial Valvotomy, with Notes on the Clinical Assessment of Patients Before and After Operation**

R. D. Rowe, S. C. Mitchell, J. D. Keith, W. T. Mustard, and W. T. Barnes. *Canadian Medical Association Journal* [*Canad. med. Ass. J.*] **78**, 311–317, March 1, 1958. 4 figs., 11 refs.

At the Hospital for Sick Children, Toronto, 24 children aged 8 months to 16 years were operated upon for severe pulmonary valvular stenosis, a modified Swan technique of transpulmonary-artery approach under hypothermia being employed. In 3 of the patients transventricular operations had previously been performed without relief. Cardiac catheterization was carried out before and after operation on 21 of the 24 patients.

Surface cooling to 30° C. or above was accomplished by water bath and ice cubes. A midline sternal splitting incision gave satisfactory extrapleural access to the pulmonary artery and permitted vena caval occlusion. After a Potts clamp had been applied an incision was made in the pulmonary artery about 1 cm. above the valve ring, and in a nearly bloodless field two deliberate scissor cuts out to the valve ring were made in the stenosed, cone-shaped valve. The clamp on the superior vena cava was released first to refill the heart to the pulmonary artery, this vessel then being closed; the duration of circulatory occlusion varied from 1½ to 3 minutes. The patient was then rewarmed to 34° C.

In all the 21 cases followed up cyanosis was abolished by the operation. Incompetence was not observed, and there was a reduction in right ventricular systolic pressure in all cases, the pressure in 17 patients being below 75 mm. Hg. There was one death. The over-all results were classified as "good" in 9 cases, "fair" in 8, and "poor" in 4; it is suggested that in the last group an infundibular stenosis was probably present. The authors consider that this operation is superior to the Brock transventricular procedure, and that it should be performed before the sixth year of life. *C. A. Jackson*

588. **Atrial Septal Defect in the Aged**

J. J. Kelly and H. A. Lyons. *Annals of Internal Medicine* [*Ann. intern. Med.*] **48**, 267–283, Feb., 1958. 8 figs., 16 refs.

Atrial septal defect, one of the most common forms of congenital heart disease, may permit the patient to live to old age. In this paper from the State University of New York, Brooklyn, 19 patients with this defect, 11 men and 8 women all over the age of 47, the oldest being 76 years of age, are described. Of these, 8 were admitted to hospital for reasons unrelated to their cardiac lesion, 5 had bronchopneumonia perhaps related to pulmonary plethora, and 4 had cyanosis, clubbing, and severe cardiac

symptoms; the remaining 2 patients died while under observation.

The usual physical, radiological, and cardiographic signs of atrial septal defect were found. The systolic murmur and early systolic click in the pulmonary area can be present with normal pulmonary blood flow, and structural alteration of the vessels may be a necessary factor in their production. The wide splitting of the second heart sound is probably caused by an increased right ventricular blood volume rather than by right bundle-branch block. Atrial fibrillation was present in 14 patients, but it is rare in younger patients with this defect. The increase in size of the pulmonary vascular tree is probably partly due to ageing of the vessels. Even when there is pulmonary hypertension the secondary branches of the pulmonary artery still remain pulsatile. Ballistocardiograms in the lateral plane showed large systolic impulses caused by the movement of large volumes of blood within the thorax. Lutembacher's syndrome was not found. In 7 cases there was pulmonary hypertension, but 2 patients over 70 years had high pulmonary blood flow with normal pulmonary vascular resistance. In a few cases pulmonary venous blood was slightly unsaturated. Respiratory infections were frequent, 7 of the patients had signs of chronic bronchitis and emphysema, and thrombosis of major pulmonary arteries occurred in 2 patients. Despite these hazards a long, active life is led by many patients with atrial septal defect. *D. Emslie-Smith*

ENDOCARDIUM

589. **Right-sided Bacterial Endocarditis and Endarteritis. A Clinical and Pathologic Study**
R. C. Bain, J. E. Edwards, C. H. Scheifley, and J. E. Geraci. *American Journal of Medicine* [*Amer. J. Med.*] **24**, 98–110, Jan., 1958. Bibliography.

From the records of the Mayo Clinic for the period 1911–55 23 cases of bacterial endocarditis with predominant or sole involvement of the right heart were obtained, and on this basis the clinical and pathological picture of right-sided endocarditis is defined. Factors influencing the development and localization of bacterial endocarditis and endarteritis are discussed.

In 19 of the cases the vegetations involved the right side of the heart or pulmonary artery exclusively, while in the other 4 cases there were lesser vegetations on the left side as well. Three patients were less than 2 years old, which supports the evidence provided by other authors that right-sided endocarditis is relatively more frequent in infants than in adults. It is also of interest that each child had a septic skin lesion, a pyogenic staphylococcal infection, and isolated tricuspid endocarditis. *Staphylococcus pyogenes* was the responsible organism in 11 cases, and for 45% of the cases occurring before penicillin was first used in 1945, but for 75% after 1945. The 3 cases of pneumococcal infection all occurred before 1945. In 16 cases the illness was regarded as acute, and virulent organisms were isolated from a high proportion of these cases, though there was no close relation between virulence and severity. Of the 7 subacute infections, 2 were caused by pyogenic staphylococci and one by a pneumococcus, while one of the 2 due to *Streptococcus viridans* ran a fulminant course.

Fever was the most prominent initial symptom, sometimes with cough or dyspnoea. Pulmonary symptoms were present at some time in 18 cases, and signs of infarction were common. Radiological changes, present in 14 out of 17 cases, were usually interpreted as due to pulmonary infiltration or pneumonitis. Cardiac murmurs were recorded in only 8 cases in all, and in only 3 of the 15 with tricuspid endocarditis and 2 of the 5 with pulmonary valvulitis [the frequency of acute illness and the infrequency of diagnosis during life possibly being relevant here]. Peripheral embolism was very uncommon, but blood cultures were positive in 17 out of 18 cases (13 of the 14 cases of isolated right-sided endocarditis), and multiple abscesses developed in 9. Splenomegaly was apparent in only about a quarter and clubbing was not present in any. Albuminuria, pyuria, and microscopic haematuria were common.

At necropsy rheumatic valvulitis was present in only one and congenital abnormalities in only 4 cases (but were more commonly associated with subacute endocarditis). Cardiac enlargement and myocardial lesions were infrequent. Septic pulmonary infarction was an almost constant finding and, with septicaemia, was the most usual cause of death. Suppurative nephritis was the most common renal manifestation, especially when *Staph. pyogenes* was the infecting organism, but focal " embolic " nephritis also occurred, and its association with exclusively right-sided endocarditis makes its embolic origin unlikely.

[This detailed paper cannot be adequately summarized.] *Celia Oakley*

590. **Short-term Penicillin and Dihydrostreptomycin Therapy of Streptococcal Endocarditis. Results of the Treatment of Thirty-five Patients**
R. Tompsett, W. C. Robbins, and C. Berntsen. *American Journal of Medicine* [*Amer. J. Med.*] **24**, 57–67, Jan., 1958. 40 refs.

This paper from the Bellevue Hospital, New York, and the New York Hospital–Cornell Medical Center records 35 cases of endocarditis due to penicillin-sensitive streptococci treated between 1949 and 1955 with penicillin (6 mega units daily) and dihydrostreptomycin (2 g. daily) given concurrently by intramuscular injection for 14 days only. The patients all had valvular or congenital heart disease and a positive blood culture (the organism in 33 cases being *Streptococcus viridans*, in one a Group-H streptococcus, and in one a microaerophilic streptococcus). All the streptococci were fully sensitive to penicillin *in vitro*. Frequent blood cultures were made for at least 3 months after completion of treatment, and most of the patients in the series are still being followed up.

In 24 cases (69%) bacteriological cure was achieved after the 14-day course. Eight others (23%) recorded as " probable bacteriological cures " included 4 patients with persistent fever despite negative blood cultures and

3 who developed an unrelated infection during the follow-up period, all needing further antibiotics. Bacteriologically proved relapse occurred in 3 patients (8·6%), one of whom relapsed twice. (The details of each case are summarized in a table and fuller details are given of those in which relapse occurred.)

The occurrence of these relapses indicates the need in some cases for prolonged treatment in order to eradicate infection in endocarditis, even when a highly effective combination of drugs is used. Presumably the size and extent of the vegetations are important in determining the effect of treatment, so it is surprising that length of illness before treatment does not seem to affect the speed of response. Suboptimal conditions slowing the rate of bacterial multiplication in the vegetations will retard the bactericidal action of penicillin. Although diffusion of penicillin and streptomycin through the vegetation is not impeded, phagocytes do not reach the bacteria lying deep to the fibrin layer until commencing organization brings new capillaries within reach. The production of highly polymerized saccharides by *Strep. viridans* and alteration of the host's immune response may also be modifying factors.

The authors conclude that their results afford additional evidence for the greater effectiveness of the penicillin–dihydrostreptomycin combination, since penicillin given alone for only 14 days results in a higher incidence of relapse. There was no significant change in sensitivity to either penicillin or streptomycin in the strains isolated following relapse, indicating that the combination prevents emergence of streptomycin resistance. While 14 days' treatment is adequate in many cases, it is still not possible to predict in which cases such short-term therapy will fail, and extension of the course to 21 or 28 days is recommended.

[There is a useful review of the literature.]

Celia Oakley

591. **Bacterial Endocarditis. Survey of Patients Treated between 1945 and 1956**

A. E. DORMER. *British Medical Journal* [*Brit. med. J.*] 1, 63–69, Jan. 11, 1958. 4 figs., 26 refs.

In an attempt to elucidate the reasons for the persisting mortality in a proportion of cases of bacterial endocarditis despite the great improvement in prognosis since the advent of antibiotics the author reviewed all the cases of the disease, totalling 82, treated at St. Bartholomew's Hospital, London, from 1945 to 1956 inclusive. The immediate mortality in this series was about 25% and there was a late recurrence rate of 18%.

The causes of death in the fatal cases are analysed and discussed at some length, and the author suggests that the mortality could be further reduced by a greater awareness of the possibility of the diagnosis and of the precipitating factors. Delay in diagnosis is still considerable, notably amongst older patients, and the risk of development of subacute bacterial endocarditis should always be borne in mind when dental or surgical treatment becomes necessary in patients with known cardiac defects. The recurrence of infection is another possibility which should not be overlooked. *J. B. Wilson*

CHRONIC VALVULAR DISEASE

592. **The Effects of Acutely Increased Systemic Resistance on the Left Atrial Pressure Pulse: a Method for the Clinical Detection of Mitral Insufficiency**

E. BRAUNWALD, G. H. WELCH, and A. G. MORROW. *Journal of Clinical Investigation* [*J. clin. Invest.*] 37, 35–40, Jan., 1958. 5 figs., 12 refs.

It has been demonstrated that in dogs with experimentally produced mitral insufficiency the left atrial pressure rises with an increase in the resistance to left ventricular ejection produced by constriction of the aorta, this finding having subsequently been confirmed in a circulatory model. These observations suggested that a similar reaction to increased systemic resistance would occur in patients with mitral regurgitation, but not in those with pure mitral stenosis, and that its demonstration might therefore be valuable in differential diagnosis.

For purposes of clinical investigation increased resistance to ventricular ejection can be produced by the infusion of noradrenaline, and the effect of this procedure on the pressure tracing recorded by cardiac catheterization from the left atrium was studied in investigations carried out on 20 patients at the National Heart Institute, Bethesda, Maryland. In 13 patients with mitral insufficiency the average ratio of the increase in the pressure at the " v " point of the left atrial tracing to the increase in systolic peripheral arterial pressure was 47% compared with only 9% in 7 cases of pure mitral stenosis. The increase in left atrial pressure was less marked in the 6 patients with mitral stenosis as well as insufficiency than in the 7 with pure mitral insufficiency, the average ratios being 30% and 63% respectively. The clinical application of these findings to the diagnosis of mitral insufficiency is discussed. *A. I. Suchett-Kaye*

593. **Mitral Valvotomy and Pregnancy**

G. WADE, W. F. NICHOLSON, and A. M. JONES. *Lancet* [*Lancet*] 1, 559–563, March 15, 1958. 22 refs.

From the Royal Infirmary, Manchester, the authors report 12 cases in which mitral valvotomy was performed during pregnancy and 15 cases in which pregnancy occurred after valvotomy, the results in both groups being encouraging. The operation may render a woman fit to undergo a pregnancy which would otherwise be regarded as inadvisable, while its performance during pregnancy will secure relief of troublesome symptoms. In the authors' experience pregnancy does not add to the operative risk and abortion is a rare consequence of the operation.

The 12 pregnant patients with mitral stenosis were selected for operation because of nocturnal attacks of dyspnoea due to pulmonary congestion (8) or severe dyspnoea on effort (4); haemoptysis occurred for the first time during pregnancy in 3. Operation was undertaken between the 10th and the 31st weeks of pregnancy, with satisfactory effects on cardiac function in all but one case. Postoperative complications included acute rheumatism and congestive heart failure, with abortion, in one case and cerebral embolism, stillbirth, and subse-

quent death in another. Six months after operation 10 of the 11 survivors were symptom-free.

Of the 15 women who became pregnant after valvotomy, 10 had experienced a total of 15 previous pregnancies, only 7 of which had resulted in live births. After valvotomy only 4 children were lost out of 16 pregnancies, and only one of these 4 as a consequence of the cardiac condition. Complications occurring during pregnancy in this group included 3 cases of nocturnal dyspnoea, one of severe haemoptysis, one of congestive heart failure in the 15th week requiring treatment until term, and 2 of pulmonary oedema. Of the 7 patients concerned, however, the cardiac condition of 5 was unsatisfactory in that the valvotomy had been incomplete or auricular fibrillation or cardiac enlargement was present. It is emphasized that if the interval between valvotomy and pregnancy is longer than 2 years a careful reassessment of the patient's heart condition should be made. On the other hand the patient's fitness for pregnancy cannot safely be assessed sooner than 6 months after operation. *M. Maclean*

594. **Aortic Stenosis**

L. Dexter, D. E. Harken, L. A. Cobb, P. Novack, R. C. Schlant, A. O. Phinney, and F. W. Haynes. *A.M.A. Archives of Internal Medicine* [*A.M.A. Arch. intern. Med.*] **101**, 254–266, Feb., 1958. 38 refs.

Now that surgery in cases of stenosis of the aortic valve is practicable there is a need for more detailed information concerning the pathology and physiology of the disease. In this paper from the Peter Bent Brigham Hospital and Harvard Medical School, Boston, a study is presented of 13 patients with pure aortic stenosis on whom surgery was contemplated. Exhaustive clinical, radiological, and electrocardiographic examinations were carried out. Left intraventricular pressure was measured, and the cardiac output was determined by the single-injection indicator-dilution method, human serum albumin labelled with radioactive iodine (^{131}I) being used as the indicator. The effective area of the aortic valve was estimated from a formula.

Aortic stenosis was advanced in all patients and angina pectoris was present in 9. Syncope, which had occurred in 7 patients, could not be correlated with any other factor. The typical systolic murmur was present in all and was not related to the degree of stenosis. In the majority of the patients the aortic second sound was absent or diminished, blood pressure was normal, and the pulse-wave was of plateau form. The electrocardiogram showed left ventricular hypertrophy. Surprisingly little evidence of left ventricular enlargement was found on *x*-ray examination.

The cardiac output was normal or increased in all cases; the cardiac index was normal in 12 cases and slightly low in one case. Left ventricular systolic pressure was over 185 mm. Hg in 11 cases. The calculated cross-sectional area of the aortic valve averaged 0·5 sq. cm. (range 0·3 to 0·7); there was good agreement between the estimated figures and those obtained at operation or at necropsy. The average total systemic resistance was normal and the left ventricular work varied from the upper limits of normal to six times the normal. There was poor correlation between the severity of the aortic stenosis and the pulse pressure, duration of arterial systolic upstroke, and anacrotism.

The authors point out that ^{131}I-induced hypothyroidism may, by reducing the cardiac output, have a place in the treatment of aortic stenosis. *David Friedberg*

CORONARY DISEASE AND MYOCARDIAL INFARCTION

595. **Relative Significance of Heredity, Diet and Occupational Stress in Coronary Heart Disease of Young Adults, Based on an Analysis of 100 Patients between the Ages 25 and 40 Years and a Similar Group of 100 Normal Control Subjects**

H. I. Russek and B. L. Zohman. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **235**, 266–277, March, 1958. 20 refs.

The parts played by heredity, a high-fat diet, occupational stress and strain, obesity, smoking habits, and a sedentary life in the development of coronary arterial disease were studied at the U.S. Public Health Service Hospital, Staten Island, and the Brooklyn College of Medicine, New York, in 100 young adults with coronary arterial disease (89 with confirmed myocardial infarction and 11 with typical angina pectoris) and 100 subjects of the same age distribution without coronary disease. A history of cardiovascular disease in the parents was elicited from 67 of the patients with coronary disease, but from only 40 of the controls. A high-fat diet was consumed by 53 of the patients compared with 20 of the controls. Occupational stress (assessed by hours of work, secondary occupations, and unusual psychological reactions) was noted in 91 of the patients with coronary disease and 20 of the controls. Of the former group, 26 suffered from obesity compared with 20 of the controls, and 70 smoked over 30 cigarettes daily as against 35 controls. Regular exercise was taken by 58 of the patients and 60 of the controls.

The authors conclude that the three major predisposing factors in the development of coronary arterial disease in young patients are heredity, a high-fat diet, and emotional strain of occupational origin.

[The major defect in this study is the lack of a proper statistical comparison of results in the two groups.] *Marcel Malden*

596. **Characteristics of True-positive and False-positive Results of Electrocardiographic Master Two-step Exercise Tests**

E. Lepeschkin and B. Surawicz. *New England Journal of Medicine* [*New Engl. J. Med.*] **258**, 511–520, March 13, 1958. 3 figs., 34 refs.

In order to establish criteria for distinguishing between true positive and false positive results of Master's two-step exercise test for the diagnosis of coronary insufficiency, 243 apparently healthy volunteers (101 males and 142 females ranging in age from 19 to over 56) were tested at the University of Vermont College of Medicine,

Burlington. All were free from symptoms attributable to coronary arterial disease. The examination gave normal results except in 10 subjects who had hypertension. The results were then compared with those obtained in 30 patients with a history of myocardial infarction or angina who had a normal resting cardiogram and gave a positive result in Master's two-step test, the result of the test being assumed to be a true positive. The most controversial of Master's criteria is the assessment of depression of the S–T segment after exercise; this may be simulated by a downward course of the T_a segment or by superimposition of the P on the U wave, particularly at higher rates. A method was therefore devised to distinguish these false depressions from true depressions of the segment by determining it from a point situated at the intersection between the tangent of the terminal portion of the P–R segment and a vertical erected through the S–T junction.

Of the 243 apparently healthy subjects, 179 gave a negative exercise test result according to Master's criteria, while 25 gave a positive result according to Master's criteria, but a negative one if the "false" depression (according to the authors' determination) was taken into consideration; 39 gave a positive result by both criteria. These false positive results occurred mostly in women over 40 and in subjects with past or present hypertension. The following combination of criteria was found best for differentiating false from true positive results: (1) inversion of T in Lead I or depression of the S–T segment (determined as above) amounting to 0·75 mm. or more, (2) the return of the S–T segment to the baseline at this time during the second half of the Q–T interval, and (3) S–T segment depression of 0·5 mm. or more and lasting for 2 minutes or more. *A. Schott*

597. **The Fate of the Internal Mammary Artery Implant in the Ischaemic Human Heart**

A. VINEBERG and G. C. MCMILLAN. *Diseases of the Chest* [*Dis. Chest*] **33**, 64–85, Jan., 1958. 16 figs., 16 refs.

The senior author's operation for coronary insufficiency, which was first performed on man in 1950 at the Royal Victoria Hospital, Montreal, and reported shortly afterwards (Vineberg and Miller, *Canad. med. Ass. J.*, 1951, **64**, 204; *Abstr. Wld Surg.*, 1951, **10**, 118), consists essentially in freeing the left internal mammary artery from the chest wall and implanting it in a tunnel constructed in the wall of the left ventricle; blood is allowed to flow freely from the vessel into the muscular tunnel, whence it is carried away by the myocardial vessels. It is highly important that angulation of the implanted artery should be avoided, since failure to observe this technical point results in arterial occlusion by thrombosis or intimal proliferation. Since 1953 a pericardial fat pad has been used to supplement the implant operation.

The authors' experimental work on dogs has shown that significant mammary–coronary arterial anastomoses have followed this operation, but in view of contrary reports, notably by Bailey and colleagues, the present paper describes in detail the fate of the grafts in 7 ischaemic human hearts taken from patients dying at various periods ranging from 60 hours to 18 months after the operation. Only one of the grafts was thrombosed, the others remaining patent, while that in the patient who survived 18 months after implantation showed little or no evidence of intimal proliferation. Apparently communications between the implanted vessel and myocardial sinusoidal spaces are established as early as 82 hours after implantation. Arterial branching starts at about 12 days, and arteriolar communicating branches (mammary–coronary anastomoses) are developed in 3 to 4 weeks and are known to have persisted for 18 months. A review of 54 patients subjected to this operation showed that among 15 cases of angina decubitus there were 9 deaths (60%) and among 39 with no angina at rest there were only 3 deaths (7·6%), while 75% of the patients were relieved of their anginal pain. Follow-up of 49 of these patients for 6 months to 5½ years showed that of 35 who had had no angina at rest (26 of these had been totally disabled before the operation), 23 had no or only slight pain, 3 had much less pain, and 30 were able to return to work, while of the 7 survivors of 14 patients with angina decubitus, all totally disabled, 3 became free of pain or had slight pain and 4 were able to return to work after operation.

F. J. Sambrook Gowar

HEART FAILURE

598. **The Treatment of Hypertensive Heart Failure and of Hypertensive Cardiac Overload by Blood Pressure Reduction**

F. H. SMIRK, M. HAMILTON, A. E. DOYLE, and E. G. MCQUEEN. *American Journal of Cardiology* [*Amer. J. Cardiol.*] **1**, 143–153, Feb., 1958. 1 fig., 25 refs.

From the University of Otago Medical School, Dunedin, New Zealand, the authors report their experience with ganglion-blocking agents in the treatment of 310 patients with hypertensive heart disease who were followed up for periods varying from 2 to 7½ years. At first hexamethonium bromide was used; more recently the drugs were pentolinium, chlorisondamine, and mecamylamine. A reduction in systolic blood pressure to 120 to 135 mm. Hg at the trough of the fall was generally aimed at, although side-effects did not always permit this.

Many of the patients with heart failure responded satisfactorily to a reduction in blood pressure only. Of 44 with combined ventricular failure, 20 recovered without digitalis, diuretics, or severe salt restriction, as did 35 out of 41 with left ventricular failure only. Of the 50 patients with heart failure who survived, 40 are actively employed; it is therefore suggested that the view that digitalis is the "therapeutic mainstay" in this condition may need modification. Hypotensive agents, moreover, appear to reduce the number of deaths which can be directly ascribed to cardiac overloading. Of the 310 patients (85 in heart failure at the beginning of treatment, 127 with exertional dyspnoea only, and 98 without either of these conditions) 96 died during the period of the study; in only 9 of these, however, was heart failure the main cause of death. If a further 10 are taken into account in

whom heart failure was a contributory cause of death, mortality from heart failure was 6·1%, as against 25% from other causes. This figure compares favourably with that in earlier reported series which have shown that heart failure is the chief cause of death in hypertension, accounting for 40 to 50% of all deaths.

It is concluded that overloading of the heart plays a more important part in the pathogenesis of hypertensive heart failure than does irreversible myocardial change. It is suggested that this finding may provide a rational basis for the treatment with ganglion-blocking agents even of symptomless hypertension. *S. G. Owen*

BLOOD VESSELS

599. **Thromboangiitis Obliterans: a 30-year Study**
F. V. THEIS. *Journal of the American Geriatrics Society* [*J. Amer. Geriat. Soc.*] **6**, 106–117, Feb., 1958. 5 figs., 29 refs.

During the past 30 years, more than 4,000 patients were examined [at Presbyterian–St. Luke's and the Cook County Hospitals, Chicago] for peripheral arterial disease; in 139 young adults with organic arterial occlusion the diagnosis was thromboangiitis obliterans. The clinical course of the disease has improved greatly since our first cases were studied and treated in 1927. No major amputation has been necessary for the past 16 years. In patients under our observation for periods of 8 to 24 years, there has been no advance of the disease to involve other limbs to any significant degree.

Study of amputated extremities and autopsy material has demonstrated that thromboangiitis obliterans is a progressive generalized arterial disease. It initially appears in the extremities as segmental arteritis and occlusive thrombosis, and is related to atherosclerosis. Only recently, this thrombosis has been shown to be due to intramural hemorrhage and ulceration of an atheromatous plaque. Arteriograms of the arterial tree *in vivo* and in amputated extremities demonstrate extensive proximal involvement of the arteries, areas of segmental occlusion, and dilated collateral vascular channels.

Results of blood studies are equivocal. However there are definite alterations in the blood, and these may be important in interpreting the early development of extensive atherosclerosis in the absence of hypercholesterolemia and of occlusive thrombosis. Increased blood viscosity, increased hemoconcentration, rapid clotting, abnormal serum lipoprotein content, and low oxygenation of the arterial blood (as reported in the literature) may contribute to the clinical and pathologic course of the disease. Almost all deaths have been due to advanced atherosclerosis with occlusive thrombosis in vital organs.

Successful treatment depends upon effectiveness in: (1) improving or correcting the morphologic and chemical (lipid) alterations in the blood and other tissues that may contribute to the arterial disease and to the occlusive thrombosis, (2) increasing the peripheral collateral circulation, and (3) controlling infection of the involved extremity.—[Author's summary.]

600. **The Use of Plasmin in the Treatment of Intravascular Thromboses**
E. E. CLIFTON. *Journal of the American Geriatrics Society* [*J. Amer. Geriat. Soc.*] **6**, 118–127, Feb., 1958. 5 figs., 10 refs.

Writing from the Sloan–Kettering Institute for Cancer Research, New York, the author discusses the treatment of intravascular thromboses with plasmin (fibrinolysin), an enzyme of which the inactive precursor, plasminogen, is present in the plasma of most animals. Being impressed with the rapid debridement and subsequent healing achieved with plasmin in the treatment of acute and chronic abscesses and sinus cavities, the author has studied the effect of the intravenous injection of the enzyme, in combination with streptokinase as its activator, in 42 cases of thrombo-embolic disease.

The only side-effect so far noted has been pyrexia of varying severity, and this was thought to be due to impurities contained in the activator. [The paper does not contain adequate clinical details of all the cases treated, nor is the dose of plasmin given, though it is stated that it was, in most cases, inadequate by the standards established in animal experiments.]

It was found that the most satisfactory results were obtained in cases of venous thrombosis, while in certain cases of arterial thrombosis or embolism the intravenous injection of plasmin or, sometimes, its direct instillation into the affected vessel, caused separation of the thrombus from the vessel wall, making its subsequent removal easier and a recurrence of embolism less likely. Six cases are described in some detail.

[While this paper can be criticized on technical grounds, the author has succeeded in demonstrating the potential usefulness of this preparation in the treatment of thrombo-embolic disorders.] *H. F. Reichenfeld*

SYSTEMIC CIRCULATORY DISORDERS

601. **The Clinical Course and Pathology of Hypertension with Papilloedema (Malignant Hypertension)**
P. KINCAID-SMITH, J. MCMICHAEL, and E. A. MURPHY. *Quarterly Journal of Medicine* [*Quart. J. Med.*] **27**, 117–153, Jan., 1958. 30 figs., bibliography.

The authors have made a comprehensive review of all cases of malignant hypertension treated at the Hammersmith Hospital, London, in the 20 years 1935–55. These numbered 197, and pathological material was available from 124 of these. The causative lesion was essential hypertension in some 40% of the patients, chronic pyelonephritis in 20%, and chronic glomerulonephritis in 15%, the remaining cases being due to all other recognized causes of hypertension except coarctation of the aorta. It was estimated that about 1% of all patients with raised blood pressure develop malignant hypertension, but the proportion is much higher in young patients. In most cases the malignant phase occurred within 8 years of the first recognition of hypertension. The blood pressure in the malignant phase was not fixed, and the level was, in general, little higher than in non-malignant hypertension. Headache, dizzi-

ness, weight loss, added heart sounds, albuminuria, raised erythrocyte sedimentation rate, nitrogen retention, and cerebral ischaemia all occurred frequently; angina, coronary arterial disease, and dissecting aneurysm were rare. The commonest causes of death were uraemia and cardiac failure (singly or combined) and cerebral vascular catastrophies. Death occurred in 55% of untreated cases within 2 months of diagnosis, and in 90% within one year. One patient is still alive 22 years after the spontaneous disappearance of papilloedema.

The second part of the paper is devoted to an extensive account of the pathological changes encountered. The characteristic findings of proliferative endarteritis and arteriolar necrosis were most extensive and florid in patients aged 30 to 60 years with essential hypertension, and were less severe in younger patients with primary renal disease. In patients who succumbed to cerebral and cardiac complications renal vascular lesions were absent. *Bernard Isaacs*

602. **The Vascular Status of a Heterogeneous Group of Patients with Hypertension, with Particular Emphasis on Renal Function**

J. H. MOYER, C. HEIDER, K. PEVEY, and R. V. FORD. *American Journal of Medicine* [*Amer. J. Med.*] **24**, 164–176, Feb., 1958. 5 figs., 12 refs.

Renal function in hypertensive vascular disease was studied in 133 patients selected at random from a total of 1,100 treated for moderate or severe hypertension at the Jefferson Davis and Veterans Administration Hospitals, Houston, Texas, over the 6-year period 1951–6. There were 73 males and 60 females in the series, the average age for the group being 49 years (range 26 to 72 years). All the patients had a sustained blood pressure above 150/100 mm. Hg, while the average blood pressures measured in the supine and erect positions were respectively 217/132 mm. Hg and 213/135 mm. Hg. The average glomerular filtration rate was 80 ml. per minute and the average renal blood flow 743 ml. per minute, compared with normal values of 131 ml. per minute and 1,209 ml. per minute respectively. In 39 of the patients, however, the glomerular filtration rate and the renal blood flow were within normal limits. On the whole there was an inverse relationship between the diastolic blood pressure and the renal clearance value. In general, too, the higher the diastolic blood pressure the greater was the incidence of complications, particularly of cerebral vascular accidents and severe retinopathy. The age, sex, and race of the patient did not appear to influence the disease process. *K. G. Lowe*

603. **The Effect of Treatment on the Vascular Deterioration Associated with Hypertension, with Particular Emphasis on Renal Function**

J. H. MOYER, C. HEIDER, K. PEVEY, and R. V. FORD. *American Journal of Medicine* [*Amer. J. Med.*] **24**, 177–192, Feb., 1958. 10 figs., 18 refs.

A follow-up investigation is reported of renal function in 64 out of 133 hypertensive patients who had been similarly studied 2 to 5 years previously [see Abstract 602]. Of these 64 patients, 45 had been adequately treated for hypertension, but the remaining 19, for various reasons, had not received treatment. There was little change in the renal clearance values in the treated patients or in untreated patients with the milder degrees of hypertension, but in untreated patients with severe hypertension there was marked deterioration in renal function. In the complete series of 133 patients clinical follow-up assessment showed that the prognosis became worse as the glomerular filtration rate fell, particularly in untreated patients. Of the 44 deaths in the series, 15 were due to uraemia, 19 to cerebral vascular accidents, 3 to uraemia with cerebral vascular accidents, 2 to myocardial infarction, 2 to heart failure, and 3 to causes unrelated to hypertension; 33 of the deaths (including all those from uraemia) were in untreated patients.

In an additional group of 5 patients with unilateral renal arterial occlusion due to atherosclerosis renal function was markedly depressed as the result of damage in the unoccluded kidney. With treatment (nephrectomy, renal arterial repair, or administration of hypotensive drugs) the blood pressure was reduced and renal function improved progressively. *K. G. Lowe*

604. **Pentacynium Bis-methylsulphate (Presidal) in the Management of Hypertension**

C. S. MCKENDRICK and P. O. JONES. *Lancet* [*Lancet*] **1**, 340–343, Feb. 15, 1958. 5 figs., 12 refs.

This paper describes the results obtained in 30 consecutive patients, 17 men and 13 women aged 41 to 68 years, who were admitted to the Regional Cardiac Centre, Liverpool, with severe hypertension and treated with "presidal" (pentacynium bis-methylsulphate), a ganglion-blocking agent with apparent dissociation between its hypotensive activity and its ability to provoke ocular or gastro-intestinal disturbances. Grading of the disorder on the basis of ocular fundal changes showed that 6 had hypertension of Grade IV, 8 of Grade III, and the remainder of Grade II. After full clinical study the patients received test doses of 3 to 10 mg. of pentacynium subcutaneously. With the patients supine, doses of 10 mg. produced a mean fall in systolic pressure of 90 mm. Hg and in diastolic pressure of 40 mm. Hg, while with doses of 3 mg. the corresponding reductions were 70 and 30 mm. Hg respectively; the blood pressure began to fall after about 10 minutes and reached its lowest level in 1 to 1½ hours, returning to resting level in 6 to 24 (mean 12) hours. The response to intravenous infusion was more rapid and to oral administration considerably slower, and was more marked in the upright posture. The heart rate slowed in most cases by 10 to 15 beats per minute.

The effective oral dose was found to be 10 to 20 times the effective subcutaneous dose, and the patients were treated orally for periods ranging from 3 to 19 months, the initial dose being 50 mg. three times a day increasing by 25 mg. every 2 days until there was adequate response or until side-effects were severe. In 24 cases the response was judged to be adequate (diastolic blood pressure maintained at less than 110 mm. Hg) on daily total doses of 300 to 700 (mean 375) mg. There was little evidence of tolerance apart from a mild degree initially

in 13 patients, and there was no obvious cross-tolerance with other ganglion-blocking agents. Reserpine had an additive effect in lowering systolic and diastolic blood pressures by 10 to 20 mm. Hg. The chief side-effects of pentacynium were blurring of vision, dry mouth, and postural hypotension; constipation was less severe than with the other available ganglion-blocking agents. The selection of patients for this type of treatment is briefly discussed, and the authors conclude that the use of ganglion-blocking agents requires a considerable effort on the part of the physician " to guide the patient through the initial period of treatment, when side-effects may be troublesome ". *K. G. Lowe*

605. **Clinicopathologic Correlations of Renal Biopsies in Hypertension with Pyelonephritis**
J. C. MERRIAM, S. C. SOMMERS, and R. H. SMITHWICK. *Circulation* [*Circulation*] **17**, 243–248, Feb., 1958. 6 figs., 9 refs.

The authors have investigated the differences in the clinical state, course, and progress of two groups of sympathectomized hypertensive patients. In one group, previously reported (*Circulation*, 1957, **16**, 207; *Abstr. Wld Med.*, 1958, **23**, 187), renal biopsies had shown only arteriolar nephrosclerosis, whereas in the other, with which the present report is mainly concerned, the arteriolar sclerosis was complicated by chronic pyelonephritis. The latter condition was diagnosed purely on the biopsy findings independent of clinical information, these including the presence of irregular scars, dilated tubules with colloid protein casts, and plasma cells with other leucocytes in the stroma. The presence of plasma cells was accepted as the most important single criterion.

The study, which was carried out at Massachusetts Memorial Hospitals (Boston University School of Medicine), was based on the case records of 120 hypertensive patients, of whom 83 were followed up for more than 5 years. Comparison with the larger series of patients without pyelonephritis showed that both groups did equally well postoperatively in regard to lowering of blood pressure and improvement in ocular fundus appearances, but that in those with pyelonephritis there was a somewhat increased mortality and less improvement in the impaired renal function. In about one-third of the cases in both groups sympathectomy resulted in a lowering of the blood pressure to normal levels.
P. Hugh-Jones

606. **Serum Cholesterol in Pentolinium-treated Arterial Hypertension**
H. H. ORVIS, I. G. TAMAGNA, and J. M. EVANS. *Circulation* [*Circulation*] **17**, 176–179, Feb., 1958. 9 refs.

Since an increase in the serum lipid content is associated with atherosclerosis and the presence of the latter is associated with hypertension, the authors, working at the George Washington University School of Medicine, Washington, D.C., have sought to determine whether any measurable changes occur in the serum cholesterol level following the treatment of hypertension with pentolinium. To this end the serum cholesterol level and blood pressure of 2 male and 9 female middle-aged hypertensive patients (aged not more than 55) were measured during a control period in which they received reserpine only (0·25 to 0·75 mg. daily), and thereafter weekly or biweekly during treatment with pentolinium in doses ranging from 100 to 830 mg. daily over 12 months; a substantial fall in blood pressure occurred and was maintained in 6 of the patients as the result of this treatment.

The blood cholesterol level exceeded 250 mg. per 100 ml. in 10 of the 11 patients before treatment with pentolinium and fell by an average of 58 mg. per 100 ml. after it. Six of the patients (including 5 of those in whom successful reduction of the blood pressure was obtained) were then given a lactose placebo in place of the pentolinium, whereupon the blood pressure rose to pre-treatment levels, with a concurrent rise in the blood cholesterol level. Fat absorption studies suggested that the changes in serum lipid levels following administration of pentolinium were due to a qualitative change in absorption, the serum turbidity as shown by optical density 3 hours after fat ingestion being increased during the placebo period as compared with that during the period of treatment with pentolinium.
P. Hugh-Jones

607. **Sympathectomy for Raynaud's Phenomenon**
R. W. GIFFORD, E. A. HINES, and W. MCK. CRAIG. *Circulation* [*Circulation*] **17**, 5–13, Jan., 1958. 15 refs.

This paper from the Mayo Clinic presents the results of a follow-up study of 70 women with Raynaud's disease and of 54 women with secondary Raynaud's phenomenon, all treated by sympathectomy. The results were assessed 1 to 28 (mean 12) years after operation.

Raynaud's disease affecting the hands was improved or abolished for the duration of the follow-up period in 37 (54%) of 68 women (in 16 of whom the feet were also affected). This figure is based on an assessment of the over-all benefit obtained, the responses in respect of individual manifestations being analysed separately. Good results were more often achieved in patients without complications of the disease (trophic changes or scleroderma confined to the fingers) than in the complicated cases. Nearly all the patients in whom the ultimate results were poor obtained initial benefit, but relapsed within the first 2 years after operation. Most of the patients in this group underwent stellate ganglionectomy, though in 9 cases preganglionic section was carried out. No difference between the results of these procedures was noted subsequently. Of the 18 patients who underwent lumbar sympathectomy for Raynaud's disease in the feet, only one failed to obtain complete relief.

Most of the patients with secondary Raynaud's phenomenon had acrosclerosis; only 2 had occlusive arterial disease. Poor results followed sympathectomy in most cases, though good results were obtained in such conditions as acrocyanosis and chronic pernio. It is noteworthy that one-third of this group of women had died (average age at death 39 years) at the time of the follow-up.

The authors suggest that sympathectomy be reserved for patients with severe or progressing Raynaud's disease. *C. J. Longland*

Clinical Haematology

608. **Hemorrhagic Diathesis Related to Quinidine Therapy**
J. C. HUNT, M. W. ANDERSON, and D. G. HANLON. *Proceedings of the Staff Meetings of the Mayo Clinic* [*Proc. Mayo Clin.*] **33**, 87–92, Feb. 19, 1958. 28 refs.

The authors review 37 cases from the literature of haemorrhagic disorder as a manifestation of sensitivity to quinidine sulphate and describe 4 further cases. The clinical findings are usually those of acute thrombocytopenic purpura. Initial symptoms, such as weakness, fever, joint and muscle pains, and pruritus, may be followed by the insidious development of mild haemorrhagic manifestations. These may, however, occur with explosive suddenness and severity, the more common ones being petechiae, ecchymoses, bleeding gums, epistaxis, gastro-intestinal haemorrhage, haematuria, and menorrhagia. Convulsive disorders may be due to intracranial haemorrhage. With repeated exposure to quinidine the severity of the symptoms increases. The haematological findings include a positive capillary fragility reaction, thrombocytopenia, prolonged bleeding time, and, rarely, leucopenia. None of the cases so far reported has been fatal. *Norval Taylor*

ANAEMIA

609. **Hemoglobin Tolerance in Various Types of Anemia**
SHU CHU SHEN. *A.M.A. Archives of Internal Medicine* [*A.M.A. Arch. intern. Med.*] **101**, 315–325, Feb., 1958. 6 figs., 26 refs.

The observation that haemoglobinaemia and haemoglobinuria are rare in patients with chronic haemolytic disease but relatively common in those with acute haemolytic anaemia prompted the investigation herein reported from Tufts University School of Medicine, Boston, Massachusetts. A slow infusion of a solution of haemoglobin derived from homologous erythrocytes was given to 18 patients with chronic haemolytic anaemia in order to test the hypothesis that such patients have an increased capacity for the uptake and catabolism of haemoglobin. Similar infusions were given to 18 patients without haemolytic disease, and in all 36 subjects the plasma levels of haemoglobin and bilirubin and the urinary excretion of the former were determined. In only 2 of the patients with haemolytic anaemia did the increase in the plasma haemoglobin level at the end of the infusion exceed 35 mg. per 100 ml., and both these patients had paroxysmal nocturnal haemoglobinuria. In contrast, in 13 control subjects without haemolytic anaemia the increase in the plasma haemoglobin level ranged from 35·9 to 66·5 mg. per 100 ml., and in the 5 non-anaemic controls from 60·9 to 100·9 mg. per 100 ml. As expected, the plasma bilirubin level rose in all the patients after haemoglobin infusion, the rise being greatest in those with evident hepatic disease.

On the basis of these results it is calculated that haemoglobinaemia may be expected in patients with chronic haemolytic anaemia only when the rate of erythrocyte destruction is between three and five times the normal. The reason for the low haemoglobin tolerance in paroxysmal nocturnal haemoglobinuria and the part played by hepatic damage, renal siderosis, and a high saturation of the haemoglobin-binding plasma protein (haptoglobin) are discussed.

[It should be noted that throughout the text and in the citation of the paper by Laurell and Nyman (*Blood*, 1957, **12**, 493) the author refers to haptoglobin as " hepatoglobin ".] *A. G. Baikie*

610. **Characterization of the Anemia Associated with Chronic Renal Insufficiency**
J. P. LOGE, R. D. LANGE, and C. V. MOORE. *American Journal of Medicine* [*Amer. J. Med.*] **24**, 4–18, Jan., 1958. 5 figs., 38 refs.

At Barnes Hospital (Washington University School of Medicine), St. Louis, the authors have carried out a detailed investigation of the anaemia occurring in 26 patients aged from 18 to 71 years who were suffering from chronic renal insufficiency and urea retention. The anaemia was consistently normochromic and usually normocytic, but in 3 instances macrocytosis was demonstrated. The serum iron level, which was either normal or decreased, showed no relationship to the free erythrocyte protoporphyrin content, which was significantly raised in 8 (38%) of 21 patients examined. A significantly decreased utilization of radioactive iron was found in all of 7 patients investigated, but in only one was this lowered utilization associated with haemolysis. This was confirmed by subsequent studies of erythrocyte survival time in 4 of the patients, in all of whom it was normal, suggesting that the decreased utilization of iron was due to depression of erythropoiesis.

As it was observed that some patients became rapidly anaemic in the absence of any detectable bleeding, further studies were undertaken to assess the possible role of haemolysis. A slight or moderate reticulocytosis was found in all 26 patients at one time or another. In 5 instances the patient's erythrocytes showed normal survival times after transfusion into normal individuals. In one case a patient's erythrocytes showed a normal survival time in a healthy subject while rapid haemolysis of healthy transfused cells was occurring in the patient. These findings indicate the action of an extracorpuscular haemolytic component. In studies of survival time of erythrocytes from healthy subjects after transfusion into 10 of the patients, 4 showed normal values, but in 5

patients (all of whom were in the terminal phase of their illness) decreased values of from 36 to 76 days were found. In the 10th patient a mild extracorpuscular factor was evident at the time of the first transfusion, but not during a subsequent test.

The Coombs reaction was negative and serum bilirubin values were normal in all 26 patients; however, 3 patients, in all of whom an extracorpuscular factor had been found, showed increased osmotic erythrocyte fragility. Faecal excretion of urobilinogen was normal in the 5 patients tested; in only 2 cases was there any significant blood loss. It is concluded that the anaemia associated with chronic renal insufficiency is mainly due to depression of erythropoiesis. Occasionally haemolysis due to an extracorpuscular factor may contribute to the anaemia, but blood loss is seldom a significant factor.

D. G. Adamson

611. **The Anemia of Renal Failure**
J. F. Desforges and J. P. Dawson. *A.M.A. Archives of Internal Medicine* [*A.M.A. Arch. intern. Med.*] **101**, 326–332, Feb., 1958. 5 figs., 18 refs.

The pathogenesis of the anaemia of renal failure was studied in 54 patients at Boston City Hospital, for which purpose erythrocyte survival, plasma iron turnover, and mechanical and osmotic fragility of the erythrocytes were measured. There was a normal erythrocyte life-span in only 3 out of 14 patients in whom this was studied by means of radioactive chromium. In the remaining 11 patients the reduction in survival was small, and insufficient in itself to account for the anaemia of renal failure. In 3 patients in whom erythrocyte survival was determined by the Ashby technique it was found that the reduction in erythrocyte life affected donor cells as well as the recipient's own cells. The plasma iron turnover was measured in 16 patients and was found to be high in 2 and low in 10, all of whom were anaemic; it was normal in 4. There was no obvious relationship between the rate of plasma iron turnover and the pathogenesis or degree of renal failure. About half the patients had increased mechanical fragility of erythrocytes, but osmotic fragility was essentially normal. It is concluded that the common mechanism of anaemia in renal failure is a mild haemolytic process uncompensated by any increased marrow activity. *A. G. Baikie*

612. **The Problems of Pathogenesis of Aplastic Conditions of Haematopoietic Organs. (A Pathologo-anatomical Study).** (Вопросы патогенеза апластических состояний кровотворных органов (Патологоанатомическое исследование))
N. A. Kraevskii and N. S. Rozanova. *Архив патологии* [*Arh. Patol.*] **10**, 10–17, No. 2, 1958. 6 figs., 26 refs.

From the Central Lenin Institute of Haematology, Moscow, the authors report a study of 54 cases of aplastic anaemia, the majority of which presented a picture of pancytopenia. The duration of illness varied from one month to several years, and the ages of the patients (33 female and 21 male) ranged from 13 to 70 years.

The aetiology in the great majority of cases was quite obscure; in only 4 of them did aplasia develop after treatment by *x*-irradiation. Complete aplasia of the bone marrow was observed in 39 cases, in which the duration of illness was from one month to 6 years. In 7 cases which ran " a subacute and even chronic course " irregular hypoplasia of the bone marrow was found post mortem. In the 8 remaining cases, in which the course was subacute with a duration of 4 to 12 months, the bone marrow remained active but qualitatively abnormal, showing an excess of plasma and reticulum cells. The possibility of the transition of an aplastic process into reticulosis and myelomatosis is discussed.

A. Swan

613. **Perspectives of Sickle-cell Disease.** [Review Article]
J. C. S. Paterson and C. C. Sprague. *Journal of Tropical Pediatrics* [*J. trop. Pediat.*] **3**, 147–156, March, 1958. Bibliography.

614. **Results of Three Years' Experience with Microbiological Assay of Vitamin B_{12} in Serum**
G. H. Spray and L. J. Witts. *British Medical Journal* [*Brit. med. J.*] **1**, 295–298, Feb. 8, 1958. 1 fig., 12 refs.

This paper from the Radcliffe Infirmary, Oxford, summarizes the results obtained by the authors in the microbiological assay of vitamin B_{12} in the serum of patients suffering from a variety of disorders, the method employed being that of Spray (*Clin. Sci.*, 1955, **14**, 661) in which *Lactobacillus leichmanii* is used as the test organism.

In 123 normal subjects, the values ranged from 150 to 1,000 $\mu\mu$g. per ml., with a mean of 450 $\mu\mu$g. per ml. Of 94 patients with untreated pernicious anaemia values of 100 $\mu\mu$g. or less were obtained in 85 and values between 100 and 170 $\mu\mu$g. per ml. in 7, but only one of the latter (170 $\mu\mu$g.) was above the lower limit of normal; the mean value in these 92 patients was 64 $\mu\mu$g. per ml. In the remaining 2 patients the results were anomalously high. In 8 patients suffering from subacute combined degeneration of the cord abnormally low levels were obtained, but in 19 in whom this diagnosis was suspected but not confirmed the serum vitamin levels were normal. For 22 patients with megaloblastic anaemia of pregnancy the mean value was 237 $\mu\mu$g. per ml., this figure being significantly lower than the normal mean, but considerably higher than that in pernicious anaemia.

In 14 patients with macrocytic anaemia following partial gastrectomy the serum vitamin-B_{12} levels ranged from 18 to 480 (mean 164) $\mu\mu$g. per ml., and similarly low levels were found in the majority of patients who had developed megaloblastic anaemia in association with total gastrectomy, diverticulosis of the small intestine, blind loops left after surgery, the malabsorption syndrome, strictly vegetarian diets, or the use of anticonvulsant drugs. Abnormally high levels (up to 6,400 $\mu\mu$g. per ml.) were found in 5 cases of chronic myelogenous leukaemia, but not in 2 cases of the chronic lymphocytic variety. In the acute leukaemias and in

polycythaemia vera both normal and high values were found, but the highest levels in polycythaemia were much lower than those in the leukaemias. Excessively high values were also found in 2 patients with haemochromatosis. It is concluded that assay of the level of vitamin B_{12} in the serum is a useful aid to diagnosis in a number of conditions. *J. L. Markson*

615. **Pernicious Anaemia Treated Orally with "Bifacton". Refractoriness to Potent Animal Intrinsic Factor**
J. B. STOKES and W. R. PITNEY. *British Medical Journal* [*Brit. med. J.*] **1**, 322–323, Feb. 8, 1958. 6 refs.

This paper from the Royal Perth Hospital, Western Australia, describes studies with radioactive vitamin B_{12} (cyanocobalamin) in a patient referred for investigation of previously treated anaemia. Some 5 months before admission she had been treated with "bifacton" tablets (of which each contains not less than 7·5 μg. of vitamin B_{12} and 18 mg. of hog-stomach intrinsic factor concentrate), one tablet three times a day for 8 weeks. Subsequently, treatment with vitamin B_{12} given intramuscularly was resumed. The patient had a histamine-fast achlorhydria but was not anaemic.

The absorption of radioactive vitamin B_{12} was assessed by a modification of Schilling's urinary excretion test, in which carbachol was injected initially to increase the secretion of intrinsic factor and radioactivity was measured in the urine collected for two 24-hour periods from the start of the test. The test showed that the absorption of the vitamin was impaired to a degree similar to that in typical pernicious anaemia and was not increased when the dose of vitamin was mixed with 50 mg. of intrinsic factor concentrate of known potency prepared from hog stomach. Absorption, however, became normal when the dose was given together with normal gastric juice. No evidence could be found of inhibition of hog intrinsic factor by the patient's gastric juice, nor could circulating antibody to this substance be demonstrated in the patient's serum.

These findings confirm the demonstration by Schwartz *et al.* (*Lancet*, 1957, **1**, 751; *Abstr. Wld Med.*, 1957, **22**, 282) of refractoriness to animal intrinsic factor following oral therapy in pernicious anaemia, and indicate that in the treatment of this condition with vitamin B_{12} the intramuscular route is to be preferred. *J. L. Markson*

616. **Oral Treatment of Pernicious Anaemia with Vitamin B_{12} and Purified Intrinsic Factor. I. The Value of Serial Estimation of the Vitamin B_{12} Levels of Serum.** [In English]
A. KILLANDER. *Acta medica Scandinavica* [*Acta med. scand.*] **160**, 339–352, March 29, 1958. 8 figs., 27 refs.

A preparation of vitamin B_{12} (cyanocobalamin) with purified intrinsic factor from the pyloric mucosa of the pig ("bifacton") was tried in the treatment of pernicious anaemia in 24 patients at University Hospital, Uppsala. The preparation was given by mouth in tablet form, each tablet containing 7·5 μg. of cyanocobalamin and 20 to 25 mg. of intrinsic factor. Of the 24 patients, 4 were in relapse; in the remainder remissions had been induced by standard methods of treatment. A daily dose of 2 to 4 tablets resulted in a satisfactory remission in the patients in relapse. On a maintenance dose of 1 to 2 tablets daily, however, 10 of the 24 patients relapsed after 15 to 28 months, 2 developing subacute combined degeneration of the cord. All subsequently responded to parenteral administration of cyanocobalamin. Subnormal serum levels of this vitamin preceded relapse in these patients by periods varying from 4 to 22 months. In 9 of the remaining 14 patients the erythrocyte cyanocobalamin content was normal but the serum level was subnormal after 15 to 39 months on maintenance therapy; in only 5 patients in the series did both these values remain normal. Serial estimations of the serum cyanocobalamin levels therefore provide evidence of relapse before clinical and haematological signs of pernicious anaemia develop.

[These results confirm the findings of other investigators that oral preparations containing intrinsic factor and cyanocobalamin are unsatisfactory for the maintenance treatment of pernicious anaemia.] *J. L. Markson*

617. **The Erythrocyte-coating Substance in Autoimmune Hemolytic Disease: Its Nature and Significance**
H. FUDENBERG, I. BARRY, and W. DAMESHEK. *Blood* [*Blood*] **13**, 201–215, March, 1958. 3 figs., 43 refs.

In a study of the nature and significance of erythrocyte coating substance (E.C.S.), carried out at Tufts University School of Medicine, Boston, eluates of this substance were obtained from the erythrocytes of 14 patients with autoimmune haemolytic disease (A.I.H.D.); in 10 of these the auto-antibodies were of the "warm" and in 4 of the "cold" type. Eluates were also obtained from normal subjects and from patients with haematological malignant disease. The method was rigidly standardized so as to obtain a relatively constant proportion of E.C.S. in each case, and the results suggest that this object was attained. Precipitin tests were performed by adding various antiglobulin sera to the eluate material; by procedures which are fully described in the paper the nitrogen concentration in eluate "antiglobulin reactive" E.C.S. was determined. Positive precipitin test results were obtained with 6 of the "warm" antibody eluates, but with none of the "cold" antibody eluates. All 17 eluates from erythrocytes of the 10 patients with "warm" antibody A.I.H.D. gave positive results in the indirect Coombs test, whereas eluates from the control subjects, the "cold" A.I.H.D. cases, and the malignant cases gave negative results.

Previous methods (which are criticized) have failed to show a correlation between the degree of positivity in the Coombs test and the severity of the haemolytic process. The present authors have demonstrated that the erythrocyte survival (determined by means of radioactive chromium) is inversely proportional to the concentration of E.C.S. Steroid therapy, which decreases antibody production and leaves the degree of positivity in the Coombs test unchanged, reduces the amount of E.C.S. and thus lengthens the erythrocyte survival time.

In several of the idiopathic cases, but in none of the symptomatic ones, unusual electrophoretic serum pro-

tein patterns (double gamma-, alpha-, and hypogammaglobulinaemia) were obtained. There was, however, no difference in reactivity of the E.C.S. between idiopathic and symptomatic cases of A.I.H.D. When normal erythrocytes were coated with material eluted from the erythrocytes of patients with malignant haematological disease there were no positive reactions when these were tested by the Coombs method with antiglobulin sera from similar cases. It is concluded therefore that cases of A.I.H.D. of the " warm " antibody type seem to be due to an immune mechanism, while the E.C.S. seems to be of the nature of an antibody. In the " cold " antibody cases on the other hand the mechanism appears to be different, and here the protein material coating the erythrocytes does not seem to be of the nature of an antibody. *R. B. Thompson*

NEOPLASTIC DISEASES

618. **Cytomegalic Inclusion Disease in Adults. A Complication of Neoplastic Disease of the Hemopoietic and Reticulohistiocytic Systems**

R. J. PEACE. *American Journal of Medicine* [*Amer. J. Med.*] **24**, 48–56, Jan., 1958. 6 figs., 16 refs.

From the Veterans Administration Hospital, Atlanta, Georgia, the author presents a detailed clinical and pathological report on 3 cases of cytomegalic inclusion disease, a rare condition due to generalized infection with " salivary gland virus " which occurs as a terminal complication of neoplastic disease of the haematopoietic and reticulo-endothelial systems. The literature of the condition is reviewed.

In the 3 cases described, occurring in men aged 29, 31, and 36 suffering from Hodgkin's disease, leukaemia, and lymphosarcoma respectively, the lesions of cytomegalic disease were most advanced where there had been almost complete replacement of the normal structure of the spleen and lymph nodes by neoplastic tissue. This finding, the author suggests, might be due to the fact that the decrease in reticulo-histiocytic tissue lessens the host resistance and so permits the spread of a virus infection previously restricted to one tissue. Further interference with resistance of the host may also occur as a result of treatment with chemotherapeutic drugs and irradiation; in these 3 cases repeated and intensive courses of nitrogen mustard and other similar drugs had been given. *D. G. Adamson*

619. **Intrathecal Amethopterin in Neurological Manifestations of Leukemia**

J. A. WHITESIDE, F. S. PHILIPS, H. W. DARGEON, and J. H. BURCHENAL. *A.M.A. Archives of Internal Medicine* [*A.M.A. Arch. intern. Med.*] **101**, 279–285, Feb., 1958. 5 figs., 14 refs.

The incidence of neurological complications in children with acute leukaemia at the Memorial Center for Cancer and Allied Diseases, New York, is stated to be between 10% and 20%. In the experience of the present authors these complications may be first manifest during otherwise successful treatment of the disease, an observation which suggests that when antileukaemic agents are given by the usual routes and in the usual dosages they are less effective against leukaemic cells in the central nervous system than in other sites.

A number of preliminary experiments were carried out on dogs following the intrathecal administration of amethopterin; the concentrations of amethopterin in the cerebrospinal fluid (C.S.F.), blood, and urine were estimated and bone-marrow cellularity and cytology were studied. Subsequently 4 children with acute leukaemia and one with lymphosarcoma were given amethopterin intrathecally in a dose of 0·5 mg. per kg. body weight. In all 5 clinical improvement followed 4 to 10 days after the first administration. The peripheral blood picture was unaffected even when the same dose was given three times in 10 days, but megaloblastic erythropoiesis was noted in the bone marrow. The high concentration of the drug in the C.S.F. suggested that even when leukaemia is refractory to the same treatment by mouth some effect on neurological manifestations may be expected after intrathecal administration. *A. G. Baikie*

620. **Fever, Infection and Host Resistance in Acute Leukemia**

R. T. SILVER, J. P. UTZ, E. FREI, and N. B. MCCULLOUGH. *American Journal of Medicine* [*Amer. J. Med.*] **24**, 25–39, Jan., 1958. 4 figs., 15 refs.

The authors, working at the National Cancer Institute, Bethesda, Maryland, have investigated the causes of pyrexia in 36 consecutive cases of acute leukaemia by means of detailed bacteriological, viral, biochemical, and radiological studies; the patients were observed for periods up to 196 days (average 72·6 days).

Fever, defined as a rectal temperature of 38·0° C. or higher, occurred on nearly 50% of the total 2,614 patient-days and only 2 patients were afebrile throughout the period of observation. Of the 92 febrile episodes, 59 (64%) were due to proved or presumed infection, the remainder being of undetermined origin. The age of the patient and type of leukaemia did not appear to influence the incidence of fever, but there was a greater proportion of proved and presumptive infections in adults than in children. Pharyngitis, pyelonephritis, and septicaemia accounted for nearly three-quarters of the cases due to major clinical illnesses associated with proved bacterial infections, while of the presumed infections, pneumonia was the commonest. Although the predominant bacteria responsible for 44 proved infections were *Escherichia coli* and *Staphylococcus pyogenes* var. *aureus* (coagulase positive) some relatively non-pathogenic organisms such as *Staph. pyogenes* var. *albus* (coagulase negative) were sometimes present. The importance of infection in patients with acute leukaemia is emphasized by the fact that 10 of the 14 patients in this study who died during the period of observation did so as a result of overwhelming infection.

The authors consider that in patients with acute leukaemia life can be prolonged by the judicious use of intensive antibiotic treatment when infection is present, but they do not advise the use of these drugs prophylactically. *D. G. Adamson*

Respiratory System

621. **Pleural Biopsy as an Aid in the Etiologic Diagnosis of Pleural Effusion: Review of the Literature and Report of 132 Biopsies**

R. F. DONOHOE, S. KATZ, and M. J. MATTHEWS. *Annals of Internal Medicine* [*Ann. intern. Med.*] **48**, 344–362, Feb., 1958. 5 figs., 15 refs.

This paper from the District of Columbia General Hospital, Washington, D.C., reviews 132 cases in which diagnostic parietal pleural biopsy was carried out on 111 patients (83 male, 28 female) with pleural effusion. Aspiration biopsy was carried out in 78 cases and pleural tissue was obtained in 60 (77%) of these. In 21 of the 78, in which the specimen was inadequate or the changes in it non-specific, a surgical procedure was subsequently adopted, while in 33 cases only the surgical approach was used.

The 78 patients on whom aspiration biopsy was successful were divided into 3 groups, according to clinical diagnosis: (I) probably tuberculous; (II) probably malignant; and (III) indeterminate. (Cases were excluded if the cause of the effusion was obvious.) Of the 28 patients in Group I, the specimen obtained from 28 showed granulomatous changes consistent with tuberculosis, this providing the only specific evidence of tuberculosis in 19 cases. Of the 19 patients in Group II, malignant involvement was found in the biopsy tissue in only 10, although all 19 were subsequently found to have malignant disease. Of the 21 patients in Group III, a diagnosis (of tuberculosis) was established by biopsy in only 2, the remainder showing only non-specific changes. Of the 54 specimens obtained surgically, 23 showed granulomatous appearances, probably tuberculous, 5 malignant disease, and 21 non-specific changes, 4 being normal and one inadequate.

The authors consider that aspiration biopsy is preferable to the surgical approach, being less liable to complications, and no less accurate. To account for the relatively large number of cases of pleurisy with non-specific changes encountered they postulate the existence of a condition of benign pleuritis analogous to benign idiopathic pericarditis. *Denis Abelson*

622. **Effects of Smoking upon the Mechanics of Breathing. I. In Normal Subjects. II. In Patients with Cardiopulmonary Disease**

E. O. ATTINGER, M. M. GOLDSTEIN, and M. S. SEGAL. *American Review of Tuberculosis and Pulmonary Diseases* [*Amer. Rev. Tuberc.*] **77**, 1–9 and 10–16, Jan., 1958. 5 figs., 25 refs.

In the first part of this experiment, reported from Tufts University School of Medicine, Boston, on the effects of smoking on breathing the respiration of 20 normal male subjects aged between 23 and 55 years, of whom 9 were smokers and 11 non-smokers, was investigated in the supine position after meals before and after smoking one or 2 cigarettes and also during normal and voluntarily increased respiration. [It is not stated whether or not the subjects were instructed to inhale.]

The intra-oesophageal balloon method was used to measure intrapleural pressure differences, and the intra-oesophageal pressure, air flow rate, and "electrically integrated volumes" were recorded continuously, special arrangements being made to correct for changes due to the heart beats. Pulmonary elasticity was expressed as change in volume per cm. H_2O (and is referred to as "compliance", a decrease of which indicates a more rigid lung). Mechanical resistance, consisting of both resistance to air flow and "tissue deformation", was expressed in cm. H_2O per litre of air flow per second. Because of some doubt regarding the accuracy of oesophageal measurements in the supine position after the use of drugs the method was checked experimentally in dogs and man and regarded as valid.

The results indicated that, in general, the immediate effects of smoking upon the mechanics of breathing are insignificant for both smokers and non-smokers, though there were a few individual exceptions. For example, one smoker and 2 non-smokers showed considerable increase in inspiratory mechanical resistance, and 2 smokers exhibited similar increase in expiratory resistance. A significant decrease in compliance during normal breathing was revealed in only one smoker and one non-smoker. However, 2 non-smokers and 2 smokers showed diminished compliance amounting to 30 to 40% during voluntarily increased ventilation after smoking and this finding, the authors suggest, indicates that in some persons smoking may cause a degree of unequal ventilation. Neither these deviations from the general findings nor the slight changes observed in the mechanics of breathing before and after smoking were statistically significant. [The number of subjects seems much too small to permit of any authoritative conclusion.]

In the second part of this study similar investigations were carried out on 9 patients with rheumatic heart disease and 25 with chronic pulmonary disease, including 7 with chronic bronchial asthma, 8 with chronic emphysema, 5 with pulmonary fibrosis, 3 with chronic bronchitis, and 2 with other respiratory conditions. Pulmonary compliance and mean mechanical resistance throughout the inspiratory and expiratory period were determined before and after smoking one or 2 cigarettes. Roughly half of these patients were smokers and half non-smokers. In this group pulmonary compliance was significantly lower and mechanical resistance, both expiratory and inspiratory, significantly higher in the control period than in the previous group of healthy subjects. After smoking the only significant differences noted were a rise in expiratory resistance and a slight decrease in compliance in the patients with emphysema. No other well-marked change was observed in those with other pulmonary conditions, and no variations from

the normally expected decrease in compliance in patients with bronchial asthma, pulmonary emphysema, or bronchitis were found. No significant differences as between all smokers and all non-smokers were noted when controls and patients with heart disease were compared, but in patients with pulmonary disease expiratory resistance was rather higher in the smokers and the effort of breathing greater than in the non-smokers.

The authors conclude that the harmful physiological effects of smoking seen in some patients may be dependent upon individual idiosyncrasy, but that these effects may be accentuated in the presence of chronic tracheobronchial disease, such as pulmonary emphysema.

Raymond Parkes

623. **The Solitary Pulmonary Nodule. A Review of 236 Consecutive Cases, 1944 to 1956**

R. R. TAYLOR, L. N. RIVKIN, and J. M. SALYER. *Annals of Surgery* [*Ann. Surg.*] **147**, 197–202, Feb., 1958. 27 refs.

The authors have reviewed the records of 236 cases of solitary pulmonary nodule in which resection was carried out at the Fitzsimons Army Hospital, Denver, Colorado, between 1944 and 1956. All the lesions were intrapulmonary and circumscribed, and varied from 1·0 to 6·0 cm. in diameter. The ages of the patients (208 males and 28 females) ranged from 17 to 74 years. Histological examination showed that granulomata of various types, (including those due to tuberculosis, histoplasmosis, and coccidioidomycosis) formed the largest group (77·6% of the cases). Malignant tumours were present in 9·7%, benign tumours in 4·2%, and miscellaneous conditions in 8·5%. Of the 17 cases of bronchial carcinoma in the series, 4 occurred in patients under the age of 40. The authors point out that in determining the suitability for surgery of cases of solitary pulmonary nodule such factors as the age of the patient, the symptomatology, the results of skin sensitivity tests, and the radiological appearances should be considered. Most granulomata (94%) were smooth-bordered, whereas 19 out of 36 lesions (53%) with fuzziness or irregularity of the edge proved to be malignant tumours. Calcification within the nodule was noted in 58 cases, granuloma being present in all except 2 of these. *R. G. Rushworth*

624. **Laboratory Differentiation of Chronic Bronchial Disease**

W. BRUMFITT and M. L. N. WILLOUGHBY. *Lancet* [*Lancet*] **1**, 132–134, Jan. 18, 1958. 4 figs., 9 refs.

Employing a method previously described (Brumfitt *et al.*, *Lancet*, 1957, **2**, 1306), the authors studied the bronchial flora in 37 cases of chronic bronchitis, 62 cases of bronchial asthma, and 18 cases of obstructive lesions of the bronchi at St. Mary's Hospital, London. The most significant finding was the presence of *Haemophilus influenzae*, either alone (in 14 cases) or in combination with other organisms (in 5 cases), in 19 of the cases of chronic bronchitis, whereas no organism predominated in the bronchi of patients with asthma or obstructive lesions of the bronchi. Although pus cells were generally found in the sputum in cases of bronchitis, their presence did not necessarily indicate the presence of an infective lesion. *R. Hare*

625. **The Effect of Salicylates upon the Ventilatory Response to Carbon Dioxide in Patients with Pulmonary Emphysema and Hypercapnia**

P. SAMET, A. ROSENTHAL, and W. H. BERNSTEIN. *American Journal of Medicine* [*Amer. J. Med.*] **24**, 215–224, Feb., 1958. 8 figs., 18 refs.

A study is reported from the University of Miami School of Medicine, Florida, of the influence of salicylates on the depressed respiratory response to inhaled carbon dioxide (CO_2) which is a well-known feature of pulmonary emphysema with CO_2 retention. In 10 patients with this syndrome whose clinical condition was static respiratory function tests and blood gas analyses were carried out during the breathing of various concentrations of CO_2 and oxygen before and after administration of aspirin and "diamox" (acetazolamide). Salicylates, with or without acetazolamide, did not influence the response of minute ventilation, alveolar ventilation, or respiratory rate to the breathing of 5% CO_2. The decrease in ventilation which followed inhalation of oxygen-rich gas mixtures was also uninfluenced by administration of salicylates, with or without acetazolamide. The serum levels of salicylate during these tests varied from 11 to 30 mg. per 100 ml.

Bernard Isaacs

626. **The Emphysema Response to Forced Straining (Valsalva's Maneuver)**

H. MILLS and A. A. KATTUS. *Circulation* [*Circulation*] **17**, 65–71, Jan., 1958. 4 figs., 23 refs.

The determination of the effect of Valsalva's manœuvre upon the blood pressure has recently been advocated as an aid in the diagnosis of certain circulatory diseases, but little attention has yet been paid to the manner in which pulmonary diseases may modify the results. At the Veterans Administration Center and University of California Medical Center, Los Angeles, the blood pressure of 29 patients with emphysema was recorded during and after forced straining, the results being compared with those from 9 healthy subjects and 80 patients with various cardiac diseases. During the performance of Valsalva's manœuvre a fall in systolic, diastolic, and pulse pressure occurs in nearly all subjects. The response of the emphysematous patients was characterized by a very marked fall in the pulse pressure, frequently to the point of obliteration, and by a marked delay in the return of the systolic pressure to the control level. The former, which is simply an exaggeration of the normal response, is attributed to a sharp diminution in cardiac output, and various possible mechanisms are discussed. The changes were most marked in those patients who had a low cardiac output and a small pulmonary blood volume.

D. Goldman

627. **Environmental Factors in Respiratory Disease.** [Milroy Lectures, 1957]

D. D. REID. *Lancet* [*Lancet*] **1**, 1237–1242 and 1289–1294, June 14 and June 21, 1958. 8 figs., 35 refs.

Otorhinolaryngology

628. **Conductive Deafness in Children**
R. E. Wehrs and G. O. Proud. *A.M.A. Archives of Otolaryngology* [*A.M.A. Arch. Otolaryng.*] **67**, 16–19, Jan., 1958. 7 figs., 6 refs.

In the treatment at the University of Kansas Medical Center, Kansas City, of 72 children with audiographic evidence of conductive deafness the authors performed adenoidectomy, removing all adenoid tissue and the lateral pharyngeal bands under direct vision, and at the same time carried out bilateral myringotomy, regardless of the appearance of the tympanic membranes. In every case fluid was found in the middle ear and removed by suction, a double incision being made so that air could enter the middle ear to replace the fluid. The nature of the fluid removed varied with the duration of the disability. In early cases it was thin and clear and in later cases thick and tenacious, or had even become jelly-like, this change being attributable to the absorption of water and the corresponding increase in the protein content.

The authors conclude that "an overwhelming majority" of children with conductive deafness also have a middle-ear effusion, and that such an effusion may be present although the tympanic membrane appears normal. Although it may well be that in many early cases the fluid is sufficiently thin to escape from the middle ear with no more help than the removal of the adenoid mass, they consider it advisable and justifiable to perform myringotomy with spot suction together with adenoidectomy on all such children. *F. W. Watkyn-Thomas*

629. **Serous Otitis Media. Treatment with Injectable Trypsin**
M. M. Auslander. *A.M.A. Archives of Otolaryngology* [*A.M.A. Arch. Otolaryng.*] **67**, 24–27, Jan., 1958. 17 refs.

Although in many cases serous otitis media clears up with myringotomy and politzerization, in others multiple incisions (sometimes as many as 40) are required and the condition becomes chronic, in some cases resulting in destruction of bone in the mastoid process which necessitates open operation. The present author attributes such chronicity to excess production of fluid by the mucosa of the middle ear and mastoid cells. In 106 cases seen in the past 2 years he has combined myringotomy, suction, and politzerization with the intramuscular injection of a trypsin preparation, which, it is claimed, reduces inflammatory oedema and promotes drainage. In 89 cases this combined treatment was immediately successful, while in the remaining 17 cases a second myringotomy was needed, though all had responded and were free of fluid by the 5th day. Like Wehrs and Proud [see Abstract 628] he has noticed differences in the consistency of the fluid withdrawn and agrees that this may be one factor affecting its escape, though in his opinion the principal factor is swelling of the mucosa. He claims that treatment with trypsin not only increases the permeability of the Eustachian tube, but also reduces the viscosity of the retained fluid. [The ages of the patients treated are not stated.]

F. W. Watkyn-Thomas

630. **Preventive Dissection of the Neck in Cancer of the Larynx**
F. J. Putney. *Annals of Otology, Rhinology and Laryngology* [*Ann. Otol. (St Louis)*] **67**, 136–144, March, 1958. 5 refs.

Preventive block dissection of the neck was undertaken 236 times as part of the surgical removal of carcinoma of the larynx. The dissection was carried out on one side only if there were no palpable lymph nodes (62 cases), but if lymph nodes could be felt (174 cases) block dissection of the second side was performed later. Of these cases, no cancer was found by the pathologist in 8% when the tissue removed by block dissection was examined, but in contrast cancer was confirmed histologically in 26% of cases without palpable lymph nodes. Of the whole series metastases were present in 56%. The highest percentage occurred in extensive lesions of the larynx and in those involving the arytenoids, the aryepiglottic fold, the pyriform fossa, and the vallecula.

Block dissection of the neck is advised as part of the operation of removal of carcinoma of the larynx because it does not materially increase the mortality or morbidity and the slight extra risk is outweighed by the advantage to the patient in terms of longer survival.

William McKenzie

631. **Elongated Styloid Process. Symptoms and Treatment**
W. W. Eagle. *A.M.A. Archives of Otolaryngology* [*A.M.A. Arch. Otolaryng.*] **67**, 172–176, Feb., 1958. 5 figs., 3 refs.

The author claims to have identified two syndromes caused by an elongated styloid process. In the first persistent pain and discomfort in the throat occur after tonsillectomy owing to stimulation of the pharyngeal endings of the 5th, 7th, 9th, and 10th cranial nerves, which become bound down by scar tissue over the tip of the elongated styloid process. In the second syndrome pain occurs in the region of the carotid artery in the neck, with or without extension into the face or head; this is due to pressure on either the internal or external carotid by the tip of the elongated styloid process. Elongation of the styloid process appears to be abnormally frequent in hypertensive patients, but the significance of this finding is not known.

The author describes an operation for removal of the elongated styloid which he has performed in more than 150 cases. In no case was there any postoperative infection of the parapharyngeal space, and in all cases the symptoms were relieved. *F. W. Watkyn-Thomas*

Urogenital System

632. **Physiopathological Aspects of Acute Diffuse Glomerulonephritis in Its Initial Stages.** (Aspetti fisiopatologici della glomerulonefrite acuta diffusa negli stadi inizali)
D. CORÀ. *Rivista critica de clinica medica* [*Riv. crit. Clin. med.*] **57**, 181–198, Oct. 31, 1957 [received Feb., 1958]. Bibliography.

At the Institute of Pathology of the University of Padua renal clearance tests were carried out on 6 patients with early acute diffuse glomerulonephritis. All were males aged between 17 and 33 and all were seen within a few days of the onset of symptoms. The detailed results are tabulated. Glomerular filtration rates were normal or slightly decreased, while renal plasma flow was normal or increased. The filtration fraction was subnormal in 4 cases and at the lower limit of normal in 2. No relationship was found between the glomerular filtration rate and the degree of oedema or level of blood pressure. The blood urea content was raised in 4 patients to a level higher than would be expected from the glomerular filtration rate. The significance of the findings are discussed and the literature is reviewed.

David Friedberg

633. **Clinical and Histological Spectrum of the Nephrotic Syndrome**
L. B. BERMAN and G. E. SCHREINER. *American Journal of Medicine* [*Amer. J. Med.*] **24**, 249–267, Feb., 1958. 22 figs., bibliography.

At Georgetown University Medical Center, Washington, D.C., specimens of kidney tissue from 45 patients with the nephrotic syndrome were examined histologically and the findings correlated with the clinical and laboratory data. The specimens were obtained by biopsy in 36 cases and at necropsy in 9. The authors define the nephrotic syndrome as a " clinical state characterized by excretion into the urine of 3·5 g. or more of protein per day, together with double refractile or oval fat bodies ". Oedema, hypoproteinaemia, and hyperlipaemia are usually, but not always, present.

Histologically, there was absence of consistent or marked tubular changes. Membranous glomerulonephritis was present in 10 patients. In 17 the nephrotic syndrome had developed late in the course of chronic glomerulonephritis, when hypertension and azotaemia were already established; these patients had widespread obliteration of glomeruli, and superadded pyelonephritis was common. In 4 further patients the nephrotic syndrome developed immediately following the acute stage of glomerulonephritis. The prognosis in this last group was poor; extensive glomerular changes, including fibrinoid necrosis and crescent formation, were present in all. Kimmelstiel–Wilson's disease, with the typical nodular lesions in the glomeruli, was found in 3 patients and amyloid disease in 4. Systemic lupus erythematosus, with glomerular changes ranging from a simple membranous glomerulonephritis to a necrotizing process, was seen in 4 patients; " wire-looping " was uncommon and the picture was sometimes indistinguishable from post-streptococcal glomerulonephritis. One patient had sickle-cell disease and one a focal membranous glomerulonephritis. The biopsy material from the remaining patient, who probably had bilateral renal vein thrombosis, was normal.

Discussing treatment of the nephrotic syndrome, the authors state that steroids may produce a remission in membranous glomerulonephritis and systemic lupus erythematosus and in selected cases of chronic glomerulonephritis, but they are contraindicated in the presence of widespread irreversible glomerular destruction causing azotaemia.

The cause of the nephrotic syndrome may be a defect of the glomerular membrane common to all the observed histological patterns, but undetectable by the conventional microscope.

T. B. Begg

634. **Adrenocorticotropin and Corticoid Treatment of the Nephrotic Syndrome.** [Review Article]
H. C. GOODMAN and J. H. BAXTER. *Metabolism* [*Metabolism*] 7, 40–51, Jan., 1958. 2 figs., 46 refs.

635. **Urinary Findings Diagnostic of Pyelonephritis**
G. G. JACKSON, H. G. GRIEBLE, and K. B. KNUDSEN. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **166**, 14–17, Jan. 4, 1958. 1 fig., 10 refs.

Chronic pyelonephritis is difficult to diagnose during life; in half the cases it is mis-diagnosed clinically as uraemia. In this paper from the University of Illinois College of Medicine, Chicago, the authors describe the preoperative findings in the urine of 71 patients subjected to nephrectomy for various forms of renal disease. Microscopic evidence of pyelonephritis was present in 42, and of these 78% had pyuria—more than 10 pus cells per high-power field in 58% and less than 10 pus cells in 20%. In 22% of the cases with pyelonephritis no pus cells were seen at one examination. Microscopic haematuria was uncommon in patients with pyelonephritis. Some degree of proteinuria was present in 65% of the latter group, but more than half of these excreted only trace amounts.

It is concluded that pyuria, the absence of microscopic haematuria, and a low degree of proteinuria are characteristic but not specifically diagnostic of chronic pyelonephritis.

K. Whittle Martin

636. **Functional Disorders of the Urinary Bladder.** [Review Article]
H. S. TALBOT. *New England Journal of Medicine* [*New Engl. J. Med.*] **258**, 643–648, March 27, 1958. Bibliography.

Endocrinology

637. **The Autoantibody Nature of the Thyroiditis Antibody and the Role of Thyroglobulin in the Reaction**
E. WITEBSKY, N. R. ROSE, and S. SHULMAN. *Lancet* [*Lancet*] **1**, 808–809, April 19, 1958. 15 refs.

On the basis of numerous animal experiments carried out by the senior author and various colleagues, in which it was shown that in rabbits, dogs, and guinea-pigs the intradermal injection of thyroid extract from an animal of the same species engendered an organ-specific thyroid antibody as well as causing thyroiditis, and in view of the demonstration (*J. Amer. med. Ass.*, 1957, **164**, 1439; *Abstr. Wld Med.*, 1958, **23**, 117) that the serum of some patients with chronic non-infective thyroiditis contains a factor which reacts with normal or goitrous thyroid extract, it is suggested that the antibody in thyroiditis is a true auto-antibody rather than an iso-antibody.

If this is in fact so, it would react with the patient's own tissues, and in this paper from the University of Buffalo School of Medicine, New York, the authors report a case in which antibodies developed 4 months after the removal of a large colloid goitre. Further, these antibodies in the patient's serum agglutinated normal human erythrocytes coated with a saline extract of the patient's own goitre (this having been stored in a frozen state), as well as erythrocytes coated with a similar extract of a goitre from another patient. In order to establish the responsible constituent in the thyroid extract fractionation with ammonium sulphate was undertaken and the antigen content of the various thyroid fractions assessed by agglutination-inhibition tests. These showed that the antigen involved was precipitated in the thyroglobulin fraction, the supernatant and the thyro-albumin fraction showing relatively little activity.

B. M. Ansell

638. **Results of 3,000 Thyroid Function Tests with Radioactive Iodine.** (Résultats de 3,000 tests d'exploration fonctionnelle de la thyroïde par l'iode radioactif)
M. TUBIANA, R. BONNIOT, X. GELLE, J. DUTREIX, and B. PIERQUIN. *Presse médicale* [*Presse méd.*] **66**, 64–67, Jan. 15, 1958. 10 figs., 16 refs.

The authors review the results of a series of nearly 3,000 tests of thyroid function with radioactive iodine (^{131}I) carried out on adults between January 1, 1951, and April 1, 1956, at the Hôpital Necker, Paris, and the Institut Gustave-Roussy, Villejuif, Seine. The uptake of ^{131}I by the thyroid gland was estimated 6 and 24 hours after the administration by mouth of a standard dose, which in 1950 was 100 μc., though improvement in the sensitivity of the Geiger–Müller counter enabled it to be reduced progressively to 15 μc. by 1953. The patients examined were divided on clinical grounds into six groups: severe hyperthyroidism (33); hyperthyroidism (533); suspected hyperthyroidism (623); euthyroid subjects (1,357); suspected hypothyroidism (269); and hypothyroidism (106). The size of the thyroid gland was estimated clinically in each case.

Analysis of the results for euthyroid subjects, 1,000 of whom were women and 357 men, showed that with increasing age the uptake of ^{131}I tended to diminish; thus 6 hours after the dose the average uptake in adolescents was about 40% of the dose and in persons over 70 30% or less. It was also found that the uptake of ^{131}I increased with the estimated weight of the gland.

The increased ^{131}I uptake by hyperthyroid as compared with euthyroid subjects was more marked after 6 hours than after 24 hours. The amount of increase was closely correlated with the severity of certain signs and symptoms, notably thirst, " thermophobia ", eye-signs, and loss of weight. About 10% of hyperthyroid subjects were found to have normal or reduced ^{131}I uptake, while the same proportion of subjects with hypothyroidism had a normal or increased rate of uptake. Such cases often provide a difficult problem in assessment.

[For detailed analyses of the findings in each group the original paper should be consulted.]

V. C. Medvei

639. **The Effect of Human Growth Hormone in Man**
D. IKKOS, R. LUFT, and C. A. GEMZELL. *Lancet* [*Lancet*] **1**, 720–721, April 5, 1958. 2 figs., 3 refs.

Growth hormone from animal pituitary glands is usually ineffective in man, probably because there are chemical differences between the human hormone and that from other animals. In this experimental study reported from Serafimerlasarettet, Stockholm, 2 male volunteer patients were given intramuscular injections of purified growth hormone prepared from human hypophyses, the dosage being 10 mg. daily for 10 and 16 days respectively. One man had been treated for obesity and the other for rheumatoid arthritis some years previously.

In both men the nitrogen, phosphorus, and potassium balances were positive during treatment. The nitrogen retained corresponded to about 1·3 kg. of fat-free protoplasm, the phosphorus retention was about equal to the calculated amount, but the potassium retention was in excess, corresponding to 1·3 and 0·5 kg. of " wet glycogen " in the 2 cases respectively. Urinary calcium excretion was increased in both cases, but calcium excretion in the faeces was increased in one and reduced in the other. Sodium and chloride were retained in both cases and the volume of extracellular fluid was increased. In one patient urinary acetone excretion was increased and the previously abnormally high urinary creatine excretion fell to normal. Both subjects showed increased perspiration, nervousness, tachycardia, and consumption of water, but a decrease in the volume of urine. The blood pressure was not affected.

Peter C. Williams

640. **Effect of Human Growth Hormone in Hypophysectomised Diabetic Subjects**
R. LUFT, D. IKKOS, C. A. GEMZELL, and H. OLIVECRONA. *Lancet* [*Lancet*] **1**, 721–722, April 5, 1958. 3 figs., 6 refs.

Human growth hormone [see Abstract 639], having been shown to be metabolically active in man, was given to one male and 2 female diabetic patients who had been subjected to hypophysectomy 4, 3½, and 3½ years previously respectively. As before, the dosage was 10 mg. of the purified human hormone daily by intramuscular injection. In all 3 patients the blood sugar level increased and glycosuria and acetonuria developed. In 2 of the cases the treatment produced such rapid deterioration of the patient's condition that extra insulin had to be given and administration of the hormone stopped after 36 hours. The effects were milder in the third case, but here, too, the treatment had to be withdrawn after 8 days.

Peter C. Williams

641. **Influence of Position and Activity on the Secretion of Aldosterone**
A. F. MULLER, E. L. MANNING, and A. M. RIONDEL. *Lancet* [*Lancet*] **1**, 711–713, April 5, 1958. 5 figs., 9 refs.

At the University of Geneva the authors have studied the diurnal and nocturnal excretion of aldosterone in the urine in 3 healthy individuals (one man and 2 women) in various positions and states of activity. They found that activity in the erect position increased the urinary excretion of aldosterone, this probably being due to a contraction of the effective blood volume. No clear-cut relationship between the excretion of sodium and aldosterone was found, since the changes in sodium excretion were affected by renal mechanisms as well as changes in aldosterone secretion. In a patient with pituitary insufficiency there was no diurnal rhythm in aldosterone excretion despite changes in posture and activity. In this subject treatment with prednisone restored the greater excretion by day provided that he was erect and active, but not when he was recumbent for 48 hours.

F. W. Chattaway

642. **Adrenocortical Insufficiency with Normal Basal Levels of Urinary 17-Hydroxycorticoids: Diagnostic Implications**
N. A. HAYDAR, J. R. ST. MARC, W. J. REDDY, J. C. LAIDLAW, and G. W. THORN. *Journal of Clinical Endocrinology and Metabolism* [*J. clin. Endocr.*] **18**, 121–133, Feb., 1958. 3 figs., 16 refs.

The authors present observations on a group of 7 patients seen at the Peter Bent Brigham Hospital, Boston, who showed some of the stigmata of Addison's disease and yet had normal basal levels of 17-hydroxycorticoid excretion in the urine. These patients failed to show a rise in steroid excretion in response to 25 units of ACTH (corticotrophin) administered intravenously over 8 hours, thus demonstrating the absence of any significant adrenocortical response. The 17-hydroxycorticoids were estimated by the method of Reddy (*Metabolism*, 1954, 3, 489) and the material measured was shown chromatographically to consist largely of tetrahydrocortisone. The urinary 17-ketosteroid excretion and circulating eosinophil count exhibited a similar failure of response to stimulation with ACTH.

In 6 of the 7 patients hyperpigmentation was the initial symptom, and in 3 cases administration of cortisone decreased the amount of pigmentation. Four of the patients required maintenance therapy, and in those who had been receiving cortisone fludrocortisone was substituted in small doses to reduce the excretion of steroid metabolites of exogenous origin. Detailed case histories of all 7 patients are presented in an appendix.

Denis Abelson

DIABETES MELLITUS

643. **Serum-lipids and Blood-sugar Levels in Childhood Diabetes**
O. H. WOLFF and H. B. SALT. *Lancet* [*Lancet*] **1**, 707–710, April 5, 1958. 2 figs., 26 refs.

At the Children's Hospital, Birmingham, determinations of the serum levels of total lipid, α-, β-, and γ-lipoprotein lipid, cholesterol, esterified fatty acid, and phospholipid in 35 diabetic children in whom the disease was under good or fair control showed that the mean levels of β-lipoprotein lipid, cholesterol, and esterified fatty acid were significantly higher when the blood sugar level exceeded 200 mg. per 100 ml. than when the blood sugar level was below this value. In 3 untreated diabetic patients with moderate ketosis high β-lipoprotein lipid values were found, but these reverted to normal on establishment of control of the blood sugar level. It was also shown that in a girl aged 12 with long-standing diabetes who was admitted to hospital in diabetic coma there was a similar relationship between the β-lipoprotein lipid level and the blood sugar level, despite the presence of gangrene and peripheral neuritis. It is considered probable that the presence of β-lipoproteinaemia may predispose to the development of arterial complications in young diabetics.

F. W. Chattaway

644. **Hypoglycemic Actions of Phenethyl, Amyl-, and *iso*Amyl-diguanide**
R. H. WILLIAMS, D. C. TANNER, and W. D. ODELL. *Diabetes* [*Diabetes*] **7**, 87–92, March–April, 1958. 3 figs., 11 refs.

The mechanism of action and clinical effect of the hypoglycaemia-inducing compounds phenylethyldiguanide (PEDG) and its amyl and *iso*amyl analogues have been studied experimentally at the University of Washington School of Medicine, Seattle, in guinea-pigs. The methods are described.

It was shown in these animals that the compounds caused depletion of liver glycogen and that gluconeogenesis was reduced. There appeared to be an additional mode of action, however, since a hypoglycaemic effect could be detected even in hepatectomized animals, which was apparently due to increased glucose utilization and anaerobic glycolysis.

In preliminary clinical trials on 66 diabetic patients, although none of these drugs produced serious toxic

effects, anorexia, nausea, and vomiting developed in one-third of the patients receiving doses of 100 mg. of PEDG per day, or 200 mg. of the *iso*amyl derivative. It is pointed out that to be clinically effective both the drugs must be administered in doses above these levels. It is concluded that phenethyl- and amyldiguanide may prove to be of clinical value in the treatment of diabetes mellitus, but much further investigation is necessary to determine the value and possible hazards of this type of therapy. *Kenneth Gurling*

645. **Pathogenesis of Orinase-induced Beta-cell Degranulation**
B. W. VOLK and S. S. LAZARUS. *Diabetes* [*Diabetes*] 7, 125–128, March–April, 1958. 3 figs., 33 refs.

The studies here reported from the Jewish Chronic Disease Hospital, Brooklyn, New York, were undertaken in order to compare the morphological changes in the islets of Langerhans, particularly in the β cells, after administration of sulphonylurea compounds with those occurring after insulin-induced hypoglycaemia; the experiments were carried out on white rabbits. Some of these animals were given up to 5 units of NPH insulin twice a day for 5 days in order to induce hypoglycaemia, while others received 0·5 g. of tolbutamide ("orinase") per kg. body weight intravenously twice daily for 7 days. The pancreas was removed immediately after each animal was killed, fixed in Zenker–formol solution, and stained by various methods which are described.

Histological examination showed that the pancreatic β cells of the tolbutamide-treated animals showed extensive or even complete degranulation, whereas those of the insulin-treated group showed no such changes. It is concluded that the β-cell degranulation produced by tolbutamide cannot be due to the prolonged hypoglycaemia, but is brought about by a direct effect of the compound on the β cells, thus supporting the contention that the sulphonylurea hypoglycaemic compounds induce increased production of insulin by the pancreas.
Kenneth Gurling

646. **Residual Cerebral Lesions in Diabetics after Hypoglycaemia.** (Cerebrale Dauerschäden bei Diabetikern nach Hypoglykämie)
O. GUNTHER. *Zeitschrift für klinische Medizin* [*Z. klin. Med.*] **155**, 125–157, 1958. Bibliography.

From the University of Greifswald, East Germany, the author presents an analysis of the cerebral effects of hypoglycaemia among 10,000 patients admitted on one or more occasions (with a total of 17,179 admissions) to the Garz and Karlsburg Diabetic Clinic between 1930 and 1954. Of the 2,545 deaths occurring during this period, 13 were certainly, and 5 others probably, due to hypoglycaemia. Altogether, out of 8,065 patients receiving insulin treatment, 87 suffered unmistakable and sometimes permanent damage to the central nervous system as a result of hypoglycaemic attacks, the symptoms including pareses, epileptic attacks, psychoses and mental changes such as impairment of power of concentration or memory, disorders of speech, Parkinsonism, and disturbances of equilibrium. Hypoglycaemia seemed to be more dangerous when delayed-action preparations of insulin were used, particularly in children and especially at night, when sleep makes recognition of the impending attack almost impossible. The use of these preparations of insulin for children has therefore been discontinued in the author's clinic.

In adults it would appear that after two attacks of hypoglycaemic coma any further attack is never without permanent after-effects. The amount of insulin administered is not the only factor determining the severity of the damage; body weight, amount of residual endogenous insulin production, activity of insulin antagonists, and preceding diet and physical activity are also of importance. Some of the fatal cases of hypoglycaemic coma occurred in the years immediately after the war when malnutrition was widespread in East Germany. Cerebral oedema and meningeal haemorrhages were seen in all cases in which necropsy could be performed, but histological examination was unfortunately not carried out. *L. H. Worth*

647. **Investigation of Renal Function in 70 Diabetics by Means of a Combined Inulin and PAH Clearance Technique.** (Untersuchungen der Nierenfunktion bei 70 Diabetikern mittels kombinierter Inulin-PAH-Clearancemethode)
H. LATOTZKI. *Zeitschrift für klinische Medizin* [*Z. klin. Med.*] **155**, 158–175, 1958. 2 figs., 20 refs.

At the Garz and Karlsburg Diabetic Clinic (University of Griefswald), East Germany, renal function tests were performed on 64 patients aged 16 to 71 who had been diabetic for 5 to 43 years and who had no history or clinical signs suggestive of kidney disease. The findings were compared with those in a group of healthy subjects and patients with diabetes of short duration. The data recorded included the serum protein level and albumin: globulin ratio, serum non-protein nitrogen level, degree of retinopathy, blood pressure, degree of albuminuria, PAH clearance, and inulin clearance, the filtration factor being calculated from the clearance figures. The techniques used are described in great detail.

In the control group PAH clearance ranged from 505 to 718 ml. per minute and inulin clearance from 102 to 148 ml. per minute, the filtration factor ranging from 0·18 to 0·22. Of the 64 diabetics, the clearance values were outside these ranges in 43, of whom 36 had a degree of albuminuria exceeding 0·1 g. per litre and 38 had retinopathy. No simple linear correlation was found between the degree of abnormality observed and the patient's age, the duration of the illness apparently being a more important factor. Exceptions and inconsistencies were not infrequent—4 diabetics with markedly abnormal clearances were free from albuminuria, while 12 others aged 18 to 51 years with diabetes of 2 to 24 years' duration had developed retinopathy, yet the results of their renal function tests were within normal limits. The author considers that these clearance tests are valuable and even essential in the assessment of the status of the individual diabetic and should be performed as a matter of routine.
L. H. Worth

The Rheumatic Diseases

648. **Effect of Desacetylmethylcolchicine (Colcemide) in Acute Gouty Arthritis**
D. H. NEUSTADT. *Arthritis and Rheumatism* [*Arthrit. and Rheum.*] **1**, 91–96, Feb., 1958. 14 refs.

" Colcemid " (deacetylmethylcolchicine; demecolcine) was given during a total of 22 acute attacks of gout to 17 patients (13 men, 4 women) ranging in age from 17 to 68. A dose of 1 mg. was given hourly until the pain was relieved or gastro-intestinal symptoms supervened. Dramatic subjective improvement was noted by 15 patients in a total of 17 attacks, the total dose needed to produce clinical relief being usually 8 mg.

The gastro-intestinal side-effects observed were less severe than with colchicine. However, a warning is issued that, unlike colchicine, demecolcine may depress the bone marrow and cause granulocytopenia, and also that complete, though temporary, loss of hair is an occasional side-effect of the drug. *G. S. Crockett*

649. **Salicylates and Adrenocortical Function in Man**
R. E. PETERSON, R. L. BLACK, and J. J. BUNIM. *Arthritis and Rheumatism* [*Arthrit. and Rheum.*] **1**, 29–37, Feb., 1958. 1 fig., 29 refs.

The effect of salicylates on adrenocortical function was investigated in 5 healthy subjects and 4 patients with rheumatoid arthritis. Single doses of 3·6 to 4·2 g. of sodium salicylate given to fasting normal subjects did not alter the plasma hydrocortisone level, while in 8 subjects who were given 3 to 6 g. of sodium salicylate daily for 3 to 50 days the plasma hydrocortisone and corticosterone levels were not significantly changed. In 3 of these cases the urinary corticoid excretion fell during the period of treatment.

Administration of salicylate did not seem to alter the rate of metabolism of infused hydrocortisone or cortisone, or the rate of synthesis of hydrocortisone. In one patient in whom a satisfactory antirheumatic response had been achieved with salicylate, depression of adrenocortical function by means of fludrocortisone did not affect this response.

The results of these investigations lend no support to the theory that the salicylates owe their antirheumatic effect in man to their influence on pituitary–adrenal function. *G. S. Crockett*

650. **Streptococcal Antibodies in Rheumatic Diseases.** (Les anticorps streptococciques dans les maladies rhumatismales)
P. RAVAULT, G. VIGNON, and J. VIAL. *Revue lyonnaise de médecine* [*Rev. lyon. Méd.*] **7**, 127–136, Feb. 15, 1958.

As a further contribution to the diagnosis of rheumatic diseases—this term being used in the widest sense—the authors present the results of 671 determinations of antistreptolysin-O titre, antistreptohyaluronidase, and antistreptokinase in cases of " rheumatism " both in adults and children seen at various hospitals in Lyons; on 472 occasions all 3 antibodies were estimated simultaneously. The techniques employed are described and significant levels defined. A simultaneous rise in the level of at least two of the antibodies was regarded as a " positive response ". The possible sources of error in performing the estimations are discussed.

Of 104 normal subjects and 92 patients with non-rheumatic diseases, the antibody levels were normal in over 80%, and less than 9% showed a positive response as defined by the authors. Of 177 patients with acute or subacute rheumatic fever with carditis, a positive response was found in 60% and normal levels in 16%. When carditis was absent (127 patients) the incidence of positive responses ranged from 35 to 55%, normal levels occurring in about 30% of the patients. In other forms of rheumatism normal levels were found in 85% and a positive response in from 0 to 14% of cases. In all groups the antistreptolysin-O titre rose more readily than the other values. The authors conclude that estimation of more than one streptococcal antibody level is of considerable value in the differential diagnosis of rheumatic fever from other forms of rheumatism.

David Friedberg

651. **The Acute Effect of Acetylsalicylic Acid in Man on the Plasma Concentration of Corticoids, the Corticotropin (ACTH) Response, and Urinary Steroid Excretion**
R. F. HERNDON, S. FREEMAN, J. X. WHEELER, and F. A. LESTINA. *A.M.A. Archives of Internal Medicine* [*A.M.A. Arch. intern. Med.*] **101**, 623–629, March, 1958. 27 refs.

Investigations were carried out at the Chicago Wesley Memorial Hospital (Northwestern University Medical School) and the Veterans Administration Hospital, Hines, Illinois, into the effects of high doses of acetylsalicylic acid (aspirin) on the plasma corticoid concentration and the urinary excretion of neutral 17-ketosteroids and corticosteroids. The 63 subjects included 26 with rheumatoid arthritis, but the results in this group did not differ substantially from those in the remainder, who were healthy adults. The diurnal variation in the plasma level of corticoids was first measured in the untreated subjects and then again after the subjects had received 30 units of ACTH (corticotrophin) intravenously over the first 6 hours of the period of observation. After an interval of at least a week the same subjects were given 30 mg. of aspirin per kg. body weight at 8 a.m., 10 a.m., and noon on two consecutive days, with corticotrophin as above on the second day, and the effects of this treatment on the plasma corticoid level, the response to corticotrophin, and the urinary excretion of neutral 17-ketosteroids and free and conjugated corticosteroids were measured.

Aspirin reduced the response of the plasma corticoid level to corticotrophin infusion while increasing the

urinary excretion of corticosteroids and reducing that of 17-ketosteroids. Given alone, however, aspirin increased the urinary excretion of 17-ketosteroids and corticosteroids while producing a fall in the plasma corticoid level.

It would appear from these findings that aspirin may stimulate the pituitary gland and that this stimulation depends on a reduction in the concentration of corticoids in the plasma. In this respect at least, therefore, it would seem illogical to give salicylates and cortisone together in the treatment of rheumatoid arthritis.

G. S. Crockett

ACUTE RHEUMATISM

652. **Researches into the Pathogenesis of Recurrent Epistaxis in Patients with Rheumatic Fever.** (Ricerche sulla patogenesi dell'epistassi giovanile recidivante dei reumatici (reumatismo acuto primario o febbre reumatica))

G. C. N. Serneri and V. Bartoli. *Rivista critica de clinica medica* [*Riv. crit. Clin. med.*] **57**, 232–265, Oct. 31, 1957 [received Feb., 1958]. 2 figs., bibliography.

At the University of Florence the authors have studied the pathogenesis of recurrent epistaxis in 97 patients with a history of rheumatic fever and in 103 non-rheumatic controls. Of these 200 subjects, 85 were under 20 years of age, 84 were between 20 and 40, and 31 between 40 and 50. Approximately half the subjects in each group had had repeated idiopathic epistaxes. All were first tested with an intradermal injection of purified human haemoglobin [the exact dose is not given], this being mixed in half the cases with 0·5 mg. of hyaluronidase. The area of skin dyed after one hour was measured.

In the patients with a history of both rheumatism and epistaxis the injection of haemoglobin alone resulted in an average dyed area of 7·4 sq. mm., compared with an average area in the other subjects ranging from 4·0 to 4·6 sq. mm. When hyaluronidase was mixed with the haemoglobin the averages for all groups were similar, ranging from 7·3 to 8·9 sq. mm. The results of suction-cup tests also indicated an increase in capillary fragility in the rheumatic patients with epistaxis. Tourniquet and pinch tests gave negative results. The implications of these findings are discussed at length, the authors postulating a change in the connective-tissue ground substance in certain subjects.

David Friedberg

653. **The Decline of Rheumatic Fever. Recurrence Rates of Rheumatic Fever among 782 Children for Twenty-one Consecutive Calendar Years (1936–1956)**

M. G. Wilson, Wan Ngo Lim, and A. McA. Birch. *Journal of Chronic Diseases* [*J. chron. Dis.*] **7**, 183–197, March, 1958. 6 figs., 18 refs.

Reports from various sources have suggested a decrease in the incidence of, and morbidity and mortality from, rheumatic fever during the past 20 years, antedating in onset the introduction of antibiotics, and in this paper from the New York Hospital changes in the recurrence rate of rheumatic fever during the years 1936–56 have been studied. From the consecutive records of 782 children (370 male and 412 female) born since 1916 who had attended the Cardiac Rheumatic Clinic and had been under satisfactory supervision the age-adjusted annual recurrence rates of rheumatic fever for the ages 2 to 20 years were calculated.

There was a total of 613 recurrences and, apart from minor fluctuations, there was a significant progressive decline in the annual recurrence rate, with a slope of −0·4% per year, which was not seen in the preceding 12 years. The mean annual recurrence rate among those patients experiencing a recurrence within 2 years of the primary attack was 3 times as great as that among patients in whom there was a longer interval between attack and recurrence, although both groups showed a significant decline in recurrence rate during the period. In almost every age group the age-specific recurrence rate for the period 1916–43 was higher than that for 1944–56. While the start of the decline in the recurrence rates of rheumatic fever antedated the antibiotic era, it coincided with a progressive improvement in the standard of living in New York City since 1936 as reflected in the socio-economic grouping of the patients attending the clinic.

B. M. Ansell

654 (a). **Tissue Culture Studies of Cellular Hypersensitivity in Rheumatic Fever. I. The Response of Human White Blood Cells to Streptococci and to Crude Filtrates of Streptococcal Cultures**

L. Florio, G. Weiss, and G. K. Lewis. *Journal of Immunology* [*J. Immunol.*] **80**, 12–25, Jan., 1958. 5 figs., 38 refs.

654 (b). **Tissue Culture Studies of Cellular Hypersensitivity in Rheumatic Fever. II. The Response of Fibroblasts from Human Skin and Heart to Disintegrated Streptococci and to Crude Filtrates of Streptococcal Cultures**

G. Weiss, L. Florio, and G. K. Lewis. *Journal of Immunology* [*J. Immunol.*] **80**, 26–31, Jan., 1958. 2 refs.

654 (c). **Tissue Culture Studies of Cellular Hypersensitivity in Rheumatic Fever. III. A Reexamination of Tuberculin Hypersensitivity in Tissue Culture by a Study of the Response to Old Tuberculin of Human White Blood Cells and Fibroblasts from Human and Guinea Pig Skin**

L. Florio, G. K. Lewis, G. Weiss, and H. Olson. *Journal of Immunology* [*J. Immunol.*] **80**, 32–38, Jan., 1958. 3 figs., 8 refs.

In these three studies, reported from the University of Colorado, Denver, tissue-culture techniques were used to test the theory that rheumatic fever is associated with delayed hypersensitivity to streptococcal products of the tuberculin type. In the first paper the literature on tuberculin and streptococcal tissue responses is first reviewed and the authors' methods of study are then described [for details of which the original paper must be read]. Essentially they consisted in observing the behaviour of leucocytes from healthy and rheumatic individuals while in contact with pooled normal and rheumatic sera with and without the addition of strepto-

coccal filtrate or disintegrated streptococci, with particular reference to the migration and spindle transformation of the leucocytes. The results showed such great variability, however, that it was impossible to distinguish serum from cases of rheumatic fever from normal serum and although there was some depression of the activity of rheumatic leucocytes on exposure to streptococcal antigen, there was no consistent or statistically significant difference between the two types of cell.

In the second study the authors observed in a similar way the growth of fibroblasts from skin and from heart, using material from 43 skin biopsies and 15 auricular tips. On the average, fibroblastic growth in material from rheumatic individuals was inhibited by a lower concentration of streptococcal filtrate and disintegrated streptococci than that necessary for inhibition of normal fibroblasts, but there was considerable overlap of the results so that individual responses could not be evaluated. There was no difference between the reactions of fibroblasts from skin and from heart and no effect was observed if rheumatic serum was used rather than normal serum.

In the third study, employing similar techniques, the response of leucocytes and fibroblasts from healthy and from tuberculous subjects to various concentrations of old tuberculin was observed. No difference was found. However, the growth of skin fibroblasts from 5 guinea-pigs was inhibited by significantly smaller concentrations of old tuberculin after sensitization than before it. Even here, however, variability was so great that it was not possible always to distinguish a sensitized from a non-sensitized animal.

The authors conclude that cellular sensitivity in man, in so far as the above results support such a hypothesis, is more evident in rheumatic fever than in tuberculosis.

E. G. L. Bywaters

655. **The Practical Application and Results of the Prolonged Systematic Prevention of Recurrences of Rheumatic Fever with Continuous Penicillin Treatment.** (Remarques sur l'application pratique et les résultats de la prévention systématique prolongée des rechutes du rhumatisme articulaire aigu par la pénicillothérapie continue)

M. KAPLAN and A. FISCHGRUND. *Pédiatrie* [*Pédiatrie*] **13**, 35–41, 1958.

During the period 1951–6 inclusive 89 patients were admitted to the Hôpital Hérold, Paris, with acute rheumatism, 66 of whom remained under regular observation after their discharge. Systematic prophylaxis against relapses was instituted in 1955, since when 40 of the 66 patients, including most of those admitted since 1954 and 10 of the 25 admitted before that date, have received this treatment. The method adopted in 42 cases was to give an intramuscular injection of 600,000 units of benzathine penicillin every 10 days, while 5 patients were treated with penicillin daily by mouth and one received penicillin by mouth at first, but subsequently by injection.

No case of relapse has occurred during continued prophylactic treatment, whereas of those patients who were admitted before 1955 (totalling 56, including those not kept under observation), 17 relapsed, one twice and another 3 times. Of the 20 relapses, 9 occurred in the first 12 months after the initial attack, 15 in the first 18 months, and 18 in the first 2 years. Some of these patients had received discontinuous penicillin prophylaxis since their first attack, but none of the 11 who have been given continuous treatment since relapsing have suffered a further relapse.

A curious fact is that none of the 8 patients admitted to hospital since 1955 who, for various reasons, were not given continuous prophylaxis, has relapsed. It is suggested that this might be due to the fact that the parents had been made aware of the risk of relapse, and that in consequence any fever, sore throat, or upper respiratory infection has been energetically treated with penicillin.

C. Bruce Perry

656. **A Comparative Study of Treatment with Hormones, Salicylates, and Phenylbutazone in 631 Attacks of Rheumatic Fever Observed in Four Years.** (Étude comparée des traitements hormonaux, salicylés, et par la phénylbutazone, d'après 631 crises rhumatismales aiguës observées en 4 ans)

J. CHEVALLIER. *Revue du rhumatisme et des maladies ostéo-articulaires* [*Rev. Rhum.*] **25**, 1–17, Jan., 1958. 8 figs., 6 refs.

This paper summarizes the results of an investigation carried out at 13 French medical centres during the 4-year period 1953–6 into the treatment and subsequent course of 631 attacks of rheumatic fever, of which 497 occurred in children. Three types of treatment were used: (1) aspirin or sodium salicylate in doses of 100 to 150 mg. per kg. body weight, according to age; (2) corticosteroids, usually as prednisone, in a daily dose of 30 to 40 mg. for periods varying from 3 to 7 weeks; or (3) phenylbutazone in a dosage of 10 mg. per kg. body weight daily. In addition all the patients received intramuscularly 1,000,000 units of benzylpenicillin daily for at least 7 days. In 68% of the cases treatment was started within 2 weeks of the onset of the attack.

Joint swellings disappeared in patients in all three groups in from one to 4 days. The mean fall in temperature in the febrile cases was similar in all groups, but was slightly more rapid in those given corticosteroids. The erythrocyte sedimentation rate (E.S.R.) (Westergren's method) fell more slowly in the group treated with phenylbutazone, rates of 20 mm. or more in one hour being maintained in this group for over 6 weeks. The plasma fibrinogen level fell most rapidly in the group treated with corticoids, and this was a factor in the rapid fall of the E.S.R. As was anticipated, the cases treated with corticosteroids did not show the same rapid fall in the leucocyte count as did the other two groups. Leucopenia occurred in a few cases treated with phenylbutazone, but in no case was this severe. The antistreptolysin-O titre showed variable changes in all groups. The "rebound phenomenon" following cessation of treatment occurred less frequently in the later years of the study when the dose of prednisone was more gradually tapered off than had been the practice earlier, but in half

the cases treated with salicylates and two-thirds of those given corticosteroids there was a temporary rise in the E.S.R. when treatment ceased. No new cardiac murmurs were discovered during this period.

An analysis of cardiac abnormalities is presented [with the aid of a number of somewhat complicated tables], the general conclusion being that murmurs appearing during treatment were evenly distributed among all three groups. The majority of cases in which murmurs were present at the onset were treated with corticoids or phenylbutazone, but it was only in the former group that harsh systolic or diastolic murmurs disappeared during treatment. There were 14 cases of severe carditis, with 4 deaths. The introduction of penicillin therapy had no effect on the incidence of carditis. The complications observed were those commonly known to be associated with the drugs used. The author's general impression is that the best over-all results were obtained with prednisone, the frequency of the toxic reactions caused by phenylbutazone weighing against the otherwise excellent results obtained with this drug. *H. F. Reichenfeld*

557. **Further Studies of the Clinical Value of the Antiglobulin Consumption Test in Rheumatic Carditis and a Comparison of the Results with Those of Other Laboratory Investigations.** (Weitere Untersuchungen über die klinische Verwertbarkeit des Antiglobulin-Konsumptionstestes bei rheumatischen Herzerkrankungen und Vergleich der Konsumptionsergebnisse mit den Resultaten anderer Laboratoriumsmethoden)
K. POLZER and C. STEFFEN. *Klinische Wochenschrift* [*Klin. Wschr.*] **36**, 211–218, March 1, 1958. 17 refs.

The authors stress the urgent need for a reliable test capable of distinguishing between active and quiescent rheumatic heart disease, pointing out that 40% of clinically quiescent cases of this condition show signs of activity at necropsy or at operation for mitral valvular disease. Steffen and Schindler (*Schweiz. Z. allg. Path. Bakt.*, 1955, **18**, 287; *Abstr. Wld Med.*, 1956, **19**, 138) have previously described a test, known as the antiglobulin consumption test, which measures a serum antibody to heart tissue. In performing the test the Coombs titres of (1) a mixture of heart homogenate and normal serum and (2) a mixture of heart homogenate and the patient's serum are determined, the difference between these two titres giving an estimate of the antiglobulin consumption in the latter mixture.

In studies carried out at Hanusch Hospital, Vienna, the results of this test were compared with the clinical state of disease activity, with the clinical course, and with various other non-specific tests in 132 patients with rheumatic heart disease, 77 with other diseases, and a control group of 72 healthy subjects.

(1) Of 62 cases of rheumatic heart disease showing either clinical or post-mortem activity of the disease, the antiglobulin consumption test was positive in 52 and negative in 10. (2) Of 70 cases without such signs of disease activity, the test result was positive in 28 and negative in 42. (3) Of 24 cases of heart disease other than rheumatic, 8 gave a positive result and 16 negative. (4) Of 53 cases of various non-rheumatic diseases, 15 gave positive results and 36 negative. (5) Lastly, of the 72 healthy controls, 8 showed a positive test result and 64 a negative one. The titres in Group 1 tended to be higher than in the other groups. In this group, also, some cases showed a decrease in the titre when clinical improvement took place. In some cases in Group 2 which gave a positive test result evidence of rheumatic activity was subsequently noted histologically in material obtained at operation.

A comparison with the results of other, non-specific, tests showed no close agreement. There was, however, some agreement with the erythrocyte sedimentation rate, but none with the Weltmann coagulation band test (a protein precipitation test of a non-specific nature). In the presence of a highly positive consumption test reaction the levels of the serum α- and γ-globulin fractions tended to be raised, as shown by paper electrophoresis. The authors consider that a positive result in a series of antiglobulin consumption tests in a clinically inactive case is evidence of rheumatic activity and recommend treatment on such a basis.

[This interesting and well documented paper describes a technique which should perhaps be regarded more as a research test rather than as a diagnostic tool at the moment.] *G. Loewi*

658. **Determination of Some Streptococcal Antibody Titers and Acute Phase Reactants in Patients with Chorea**
T. N. HARRIS, S. FRIEDMAN, and D. C. MCLEAN. *Pediatrics* [*Pediatrics*] **21**, 13–21, Jan., 1958. 2 figs., 16 refs.

Previous studies of chorea have shown that only a proportion of cases of this disorder manifest signs or symptoms of rheumatic fever and that the remainder, designated " pure " chorea or " non-rheumatic " chorea, show less laboratory evidence of systemic upset and have a better prognosis. The authors have therefore studied 43 samples of serum from patients with chorea at the Children's Hospital of Philadelphia; all the sera had been taken within 2 weeks of the diagnosis of the choreic episode and stored at −5° C. Of the 43 patients, 23 had other major manifestations of rheumatic fever, while the other 20 had not. Age, race, and sex distributions were similar in the two groups. Criteria for the diagnosis of chorea were (1) involuntary movements, (2) muscle weakness, and (3) incoordination and emotional lability.

The results of determination of the erythrocyte sedimentation rate (E.S.R.) (by the O'Rourke and Ernstene method) and serum mucoprotein tyrosine content and C-reactive protein level all showed marked differences between the two groups, those in the cases of " pure " chorea being nearer the normal. A separate study showed that the 4 patients in the pure chorea group with the highest E.S.R. value also had a raised antistreptolysin-O titre. The antistreptolysin-O and antihyaluronidase titres were also lower in the pure chorea group as a whole, but the results showed rather more overlap than did the acute-phase reactions. Subdivision of the " rheumatic " chorea group into those whose chorea was part of the rheumatic episode and those whose chorea was separate in time from it showed

that there was little difference in distribution of the anti-streptococcal titre between the two subgroups. Although the work of Taranta and Stollerman is cited, the authors conclude that the symptom complex of chorea can exist apart from the disease of rheumatic fever. In view of the difficulty of distinguishing the two categories, however, they point out that this does not absolve the physician from instituting antibiotic prophylactic treatment in all cases of acute chorea. *E. G. L. Bywaters*

CHRONIC RHEUMATISM

659. **Peripheral Neuritis Associated with Rheumatoid Arthritis**

R. Irby, R. A. Adams, and E. C. Toone. *Arthritis and Rheumatism* [*Arthrit. and Rheum.*] **1**, 44–53, Feb., 1958. 4 figs., 12 refs.

In 6 cases of rheumatoid arthritis in which the disease had been present for 13 to 20 years signs of peripheral neuritis were detected. These patients, all of whom were seen during the course of 2 years and 5 of whom were male, complained predominantly of numbness, tingling, and burning of the extremities. Sensory changes were more marked than motor, and in all cases the knee-jerks were retained. The condition is considered to be due to an inflammatory lesion of the blood vessels supplying the nerves affected. All the patients had been receiving steroid therapy for some time, and there is some indication that this may be a factor in the aetiology. *G. S. Crockett*

660. **Arteriolar Involvement in Rheumatoid Arthritis.** (La sofferenza arteriolare nel reumatismo cronico primario)

G. G. N. Serneri and A. Sciagrà. *Rivista critica de clinica medica* [*Riv. crit. Clin. med.*] **57**, 211–231, Oct. 31, 1957 [received Feb., 1958]. 5 figs., bibliography.

In studies reported from the University of Florence finger plethysmography was carried out on 14 patients with chronic rheumatoid arthritis, observations being made first at ordinary room temperature (18° C.), then after immersion of the hand for 5 minutes in water at 45° C., and lastly after 5 minutes' immersion in water at 3 to 5° C. In 2 cases the tracings were normal and in 4 others there were very slight abnormalities. In the remaining 8 cases, which are reported in detail, the abnormal responses are described as of the "Raynaud type" or of the "noradrenaline type". The implications of these findings are discussed.

David Friedberg

661. **The Agglutination of Collodion Particles Sensitized with Gamma Globulin in Rheumatoid Arthritis.** (Agglutination der mit Gamma-Globulin sensibilisierten Kollodiumteilchen bei der chronischen Polyarthritis)

V. Zavázal. *Zeitschrift für Rheumaforschung* [*Z. Rheumaforsch.*] **17**, 41–46, Feb., 1958. 1 fig., 20 refs.

In this study, reported from the Institute of Immunology, Pilsen, Czechoslovakia, it was shown that collodion particles coated with normal human gamma globulin were agglutinated in 80% of 137 cases of rheumatoid arthritis. This was compared with the differential haem-agglutination test (modification of Svartz) which gave 83% positive results in the same case material. With the collodion particles, however, much higher titres were obtained in the cases of rheumatoid arthritis and also fewer false positive results in a normal control group than with the differential agglutination test. In a third group of 40 cases of miscellaneous joint disorders other than rheumatoid arthritis only 4 positive results were recorded with the collodion method against 19 with the haemagglutination test. It appears therefore that the collodion-particle method is more sensitive and more specific in the diagnosis of rheumatoid arthritis than the differential haemagglutination test. *G. W. Csonka*

662. **Bentonite Flocculation Test for Rheumatoid Arthritis**

J. Bozicevich, J. J. Bunim, J. Freund, and S. B. Ward. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. Soc. exp. Biol.* (*N.Y.*)] **97**, 180–183, Jan., 1958. 4 refs.

Particles of bentonite (a North American clay) were used by Bozicevich *et al.* (*Publ. Hlth Rep.* (*Wash.*), 1951, **66**, 806) to adsorb antigenic material from *Trichina* for use in a serological test for trichiniasis. In the present paper the authors describe the use of a slight modification of this method in the detection of the serum factor characteristic of rheumatoid arthritis, bentonite particles coated with human γ globulin (Fraction II of Cohn) flocculating when mixed with serum containing the rheumatoid factor, but not when mixed with control sera.

The stock suspension of bentonite in water is prepared by a method entailing two centrifugations [the details of which are important and should be consulted in the original]. Lyophilized Fraction II prepared from normal human serum is dissolved in veronal buffer and absorbed on to the bentonite particles, using four centrifugations with washing. The serum to be tested is first heated to 56° C. for 30 minutes and serial twofold dilutions made in saline. To 1 ml. of each dilution on a ringed slide is added one drop (about 0·025 ml.) of the suspension of sensitized particles by means of a capillary pipette; the slide is rotated mechanically 100 to 120 times per minute for 20 minutes and is then examined for flocculation under low-power magnification, the degree of flocculation being graded from 0 to 4+. The reaction is regarded as positive when 2+ or stronger clumping occurs in a serum dilution of 1:32 or higher.

Of 41 sera from adults with "unquestionable" rheumatoid arthritis, 32 (78%) gave a positive bentonite fixation reaction. There was some association of a positive reaction with the presence of subcutaneous nodules, but this was not very close. Of the 9 sera which gave a negative reaction, 6 also gave negative results in agglutination tests with sheep erythrocytes sensitized with euglobulin. Of 163 sera from normal subjects and patients with diseases other than rheumatoid arthritis, 3 gave positive reactions; one of these patients had systemic lupus erythematosus, one macroglobulinaemia, and one acute leukaemia. A direct comparison between

the results of the bentonite test and the sensitized sheep cell test was carried out on 64 sera from cases of rheumatoid arthritis, with concordance in 98%

E. G. L. Bywaters

663. **Evaluation of Haemagglutination Tests in the Diagnosis of Rheumatoid Arthritis. I. The S.S.C., F.II S.C., and F.II L.P. Systems**

H. HARTFELD, E. MAHOOD, and E. F. HARTUNG. *Annals of the Rheumatic Diseases* [*Ann. rheum. Dis.*] **17**, 83–88, March, 1958. 11 refs.

In this important contribution from the New York University–Bellevue Medical Center the results of an evaluation of three recently introduced tests derived from the Rose–Waaler sheep-cell haemagglutination phenomenon in rheumatoid arthritis are described. The aim was to determine their relative value in "the differentiation of rheumatoid arthritis from other cases appearing in an arthritis clinic".

The three tests which were chosen as being suitable for routine diagnostic purposes and performed concurrently on 239 patients (147 with rheumatoid arthritis) were: (1) the Heller I modification of the Rose test (the S.S.C. test); (2) the Cohn Fraction II modification of Heller *et al.* (F.II S.C. test) (*J. Immunol.*, 1954, **72**, 66); (3) the latex fixation test (F.II L.P.) of Singer and Plotz (*Amer. J. Med.*, 1956, **21**, 888). The results of the three tests showed agreement in 83% of cases, with a higher degree of correlation between the S.S.C. and F.II L.P. tests than between either of these and the F.II S.C. test. Of 75 cases of "classical or definite" rheumatoid arthritis, all three gave positive results in 62·8%, the S.S.C. test being positive in 66·3%, the F.II L.P. test in 68·2%, and the F.II S.C. test in 72·2%. In 46 cases of "probable" and "possible" rheumatoid arthritis all three tests consistently gave positive results more frequently than in a control group of 46 cases of non-rheumatoid and non-collagen disease. Of the latter, 8·6% gave positive results in the S.S.C. test, 4·3% in the F.II L.P. test, and 15·2% in the F.II S.C. test. It is concluded that when suitable (and possibly different) standards of positivity are used all three tests are equal in sensitivity for routine diagnostic screening. It is recommended that the lowest titre recognized as positive should be 1:448 or 1:896 in the F.II S.C. test and 1:160 in the F.II L.P. test, the latter test being preferred because of its simplicity and rapidity of performance.

Harry Coke

664. **Marrow Iron Examination in the Diagnosis of Iron Deficiency in Rheumatoid Arthritis**

P. C. MCCREA. *Annals of the Rheumatic Diseases* [*Ann. rheum. Dis.*] **17**, 89–96, March, 1958. 39 refs.

In the evaluation of iron deficiency as a factor in the anaemia commonly present in rheumatoid arthritis examination of the peripheral blood is frequently inconclusive, although the haematocrit may provide evidence of iron-deficiency anaemia. In the investigation here reported from Harrogate and District General Hospital bone-marrow specimens from the manubrium sterni or the sternum were examined in 33 cases of rheumatoid arthritis and 2 control cases of uncomplicated iron-deficiency anaemia. Sections were stained for iron by the Prussian blue method and the cytological examination was made with particular reference to the maturation of the erythroid series. In all 33 cases the mean corpuscular haemoglobin concentration was 29% or less.

In 11 cases the bone marrow was devoid of stainable iron; in 10 of these the haemoglobin level of the blood rose by 2 g. per 100 ml. or more—regarded as a "significant response"—as a result of intravenous iron treatment, 6 to 10 injections of a colloidal preparation of saccharated oxide of iron being given during a period of 8 to 14 days to an approximate total dose of 1 g. This haemoglobin response was less and the reticulocyte count lower than in the control subjects. Of the 22 cases in which stainable iron was observed in the marrow, treatment resulted in a rise in haemoglobin level of 2 g. per 100 ml. or more in only one. Cytologically, there was no marked hyperplasia of the erythroid series. In many cases an increase in basophilic normoblasts was observed which was unrelated to the presence of iron, and which is regarded as evidence of a delay in erythroid maturation. In 10 cases the proportion of plasma cells was greater than 2%, and this was constantly associated with a serum globulin level of more than 3 g. per 100 ml.

[No consideration is given to the possible significance of the known rise in the serum content of haemoglobin-combining α_2 haptoglobins in rheumatoid arthritis.]

Harry Coke

665. **Prostatitis and Ankylosing Spondylitis**

R. M. MASON, R. S. MURRAY, J. K. OATES, and A. C. YOUNG. *British Medical Journal* [*Brit. med. J.*] **1**, 748–751, March 29, 1958. 2 figs., 42 refs.

An association between prostatitis and ankylosing spondylitis is not a new finding, but it is still not clear whether the two conditions are causally related. In this paper from the London Hospital a study is reported of the incidence of prostatitis in 54 male patients with ankylosing spondylitis, 59 with Reiter's disease, and 86 with rheumatoid arthritis.

Reiter's disease was diagnosed on the presence of non-gonococcal urethritis associated with arthritis of acute onset and a variable, often relapsing, course. Conjunctivitis occurred in 24 of the 59 cases, uveitis in 6, and keratodermia blennorrhagica in 6. From each patient 5 samples of fluid were obtained by prostatic massage and examined microscopically in a high-power dark field. The criterion for diagnosis of chronic prostatitis was a minimum of 10 pus cells per high-power field. By this method chronic prostatitis was demonstrated in 45 (83%) of the patients with ankylosing spondylitis, 28 (33%) of those with rheumatoid arthritis, and 56 (95%) of those with Reiter's disease.

The authors do not consider that the difference between the groups with ankylosing spondylitis and with rheumatoid arthritis in respect of the incidence of prostatitis is due to the different mean age of the patients; there is no evidence that chronic prostatitis is commoner in

younger than in older males. The incidence of chronic prostatitis in healthy males is reported to be 20 to 25%; the incidence in rheumatoid arthritis in this series thus appears to be close to that found in the general population of the same age group.

Radiological examination of the sacro-iliac joints of all the patients revealed unequivocal bilateral sacro-iliiitis in 49 of the cases of ankylosing spondylitis, 7 cases of rheumatoid arthritis, and 19 of Reiter's disease—findings which might be taken to indicate that there is a causal association between chronic prostatitis and sacro-iliiitis. However, the authors do not find much support for this in their figures; in all 11 cases of ankylosing spondylitis with a normal prostatic fluid there was unequivocal bilateral sacro-iliiitis.

The high incidence of chronic prostatitis in ankylosing spondylitis remains unexplained. *Kenneth Stone*

COLLAGEN DISEASES

666. **Evaluation of Simple Precipitation Test for Systemic Lupus Erythematosus**
K. K. JONES and H. E. THOMPSON. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **166**, 1424–1428, March 22, 1958. 5 refs.

The authors, at the Clinical Research Laboratory, Tucson, Arizona, observed during routine determination of serum cholesterol levels that the addition of 2 ml. of a 12% solution of *p*-toluene sulphonic acid in glacial acetic acid to 0·1 ml. of serum yielded a heavy precipitate in cases of active untreated systemic lupus erythematosus (S.L.E.). In this paper they report the results of this precipitation test in patients with S.L.E. and various other diseases, as well as in healthy subjects. Of 30 patients with S.L.E., 13 were acutely ill and sera from 12 of these gave heavy precipitates (2+ to 4+). The remaining 17 patients were not acutely ill or were in remission; sera from 11 of these gave no reaction, while sera from 6 showed a slight precipitate (1+). In serial tests the degree of precipitation paralleled the clinical state of the patient. A negative result or a slight precipitation only (1+) was obtained with sera from all patients with polyarteritis nodosa, scleroderma, rheumatoid arthritis, osteoarthritis, and a variety of miscellaneous diseases and from healthy subjects. In a few cases of hepatitis and of myelomatosis, however, strongly positive results were obtained.

The nature of the precipitate has not yet been determined. *E. G. Rees*

667. **Systemic Lupus Erythematosus: a Complex Autoimmune Disorder?**
W. DAMESHEK. *Annals of Internal Medicine* [*Ann. intern. Med.*] **48**, 707–730, April, 1958. Bibliography.

The hematologic abnormalities of systemic lupus include a positive Coombs' test with or without hemolytic anemia; thrombocytopenic purpura; leukopenia, at times severe; a positive serologic test for syphilis; a hemorrhagic disorder due to circulating anticoagulants, and the L.E. factor. They may be said to be just as representative of the disease as are the " onion-skin " vascular lesions in the spleen, the " wire-loop " lesions in the kidneys, or the vascular and " collagen " lesions elsewhere. The various hematologic abnormalities, including the L.E. factor, may be considered as " auto-immune " in nature with the development of auto-antibodies against various antigens in the blood cells or plasma. The L.E. factor is probably an abnormal auto-antibody directed against a constituent of the leukocyte nucleus. Other leukocytic antibodies may also occur in the disease.

If the various hematologic lesions of systemic lupus are considered to be " auto-immune ", it is likewise possible that the vascular lesions (vasculitis), with resultant skin lesions (lupus), arthritis, nephritis, pleuritis, endocarditis, etc., may also be due to auto-antibodies, but in this instance directed against small blood vessels. Indeed, the entire disease of systemic lupus may be a complex of immunologic disturbances affecting (1) blood cells and other blood constituents, and (2) small blood vessels. The L.E. factor may be considered as only one of the immunologic abnormalities of lupus; thus, its lack in a given case does not necessarily rule out the presence of the disease.

" Idiopathic " thrombocytopenic purpura (ITP) is often a prodrome of systemic lupus—thus, every case of ITP in a young woman should be suspected of being lupus. " ITP " need not be considered to be symptomatic of lupus, but simply as one part of the generalized disease. Combinations of ITP with auto-immune hemolytic anemia are even more likely to be examples of lupus, whether or not other manifestations of systemic lupus are present. Dissemination of the lupus process may be accelerated by splenectomy.

The presence of complex mixtures of auto-antibodies in systemic lupus suggests that numerous antigens (perhaps altered blood cells, altered blood plasma constituents, altered small blood vessels) are concerned. Since the great majority of cases of the disease occur in women, the possibility is present that antigen development may take place in the menstruating endometrium. Here, at monthly intervals, alterations in blood cells, blood plasma constituents and small blood vessels (spiral arteries) take place. One may speculate that in certain women these altered cells, plasma factors and blood vessel constituents become auto-antigenic, thus leading to the formation of several types of auto-antibodies against both blood constituents and small blood vessels, and thus to the complex disease known as systemic lupus. The periodic character of the menstrual cycle might well aid in auto-antibody formation. Such a speculation does not preclude the possibility of auto-immunization by other mechanisms, as in the relatively uncommon cases in males.—[Author's summary.]

668. **Progressive Systemic Sclerosis (or Visceral Scleroderma). Review of the Literature and Report of Cases.** [Monograph. In English]
M. L. ORABONA and O. ALBANO. *Acta medica Scandinavica* [*Acta med. scand.*] **160**, Suppl. 333, 1–170, 1958. 53 figs., bibliography.

Physical Medicine

669. **Cross Exercise—a Review of the Literature and Study Utilizing Electromyographic Techniques**
F. A. GREGG, A. F. MASTELLONE, and J. W. GERSTEN. *American Journal of Physical Medicine* [*Amer. J. phys. Med.*] **36**, 269–280, Oct., 1957. 7 figs., 26 refs.

The authors, writing from Fitzsimons Army Hospital, Denver, Colorado, review the literature on the subject of "cross exercise", a term meaning the transfer of the effects of systematic exercise of muscles in one part of the body to the muscles in another part. They then describe an experiment in which 20 healthy adult subjects were connected to a multi-channel ink-writing oscillograph by surface electrodes, which were placed equidistant from the motor point of the muscle under observation, and simultaneous tracings taken from the left and right biceps and triceps muscles during exercise of the right biceps. The exercises consisted in flexion of the right elbow and extension against various graded resistances or isometric contractions while the subject lay supine with the left arm in different positions and the body either free or stabilized with straps. A total of 320 tracings were taken.

The results showed that during simple non-resisted exercise or isometric contractions of the right biceps no overflow to the unexercised contralateral muscles occurred. This did occur, however, when the exercise stress was increased, either by increasing the load or the number of repetitions, and was first noted in the opposite triceps muscle and then in the contralateral biceps; it disappeared if a maximal isometric contraction was performed or after a 2-minute rest period, but returned after a few further contractions. The position of the unexercised limb or degree of body stability did not appear to influence the overflow. The antagonist triceps muscle showed no activity unless resisted exercises or strong isometric contractions of the biceps occurred. It is suggested that there is a relationship between the appearance of such overflow, movement of a heavy load, and fatigue. *J. B. Millard*

670. **Electric Stimulation of Breathing in Chronic Lung Diseases**
G. W. HOLMES, W. B. BUCKINGHAM, D. W. CUGELL, and K. KIRCHNER. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **166**, 1546–1551, March 29, 1958. 3 figs., 17 refs.

The use of breathing exercises in certain chronic lung diseases, such as emphysema and bronchiectasis, and after operations on the lung has become almost traditional. A scientific and objective assessment of the value of such exercises is, however, difficult since it is not possible to obtain a series of comparable untreated patients as controls. The authors of this paper from the Cook County Hospital, Chicago, describe a portable apparatus which can alternately stimulate the diaphragm for inspiration and the rectus abdominis for expiration, the frequency and duration of the stimuli being adjustable. Each treatment lasts 10 to 15 minutes, and two or three treatments are given each week. The method was tried on four different groups of patients: (1) 5 patients with chronic empyema; (2) 7 patients with chronic haemothorax; (3) 9 patients with pleural exudate after undergoing lobectomy; and (4) 13 patients suffering from chronic emphysema. In all cases clinical examination, simple ventilatory tests, and *x*-ray examination of the chest were carried out before and after treatment. There was satisfactory improvement in the patients suffering from chronic empyema and in the post-lobectomy group, while the patients with chronic haemothorax "showed remarkable clinical improvement". Although there was some increase in the vital capacity of the patients with emphysema, clinical improvement in this group was not significant. *W. Tegner*

671. **Tetanizing Current in the Rehabilitation of Hemiplegics.** (Les courants excito-moteurs dans la rééducation des hémiplégiques)
S. HANOUNE. *Annales de médecine physique* [*Ann. Méd. phys.*] **1**, 47–54, Jan.–March, 1958.

At the Hôpital Beaujon, Paris, a tetanizing current has been used as an aid in the restoration of function in 103 cases of hemiplegia. It is claimed that this method of treatment is superior to all other forms of physiotherapy and, in the present series, gave results which in 12 cases are described as "spectacular", in 19 were assessed as good, in 12 as moderate, and in 19 as slight; in 28 cases there was no benefit, and the remaining 13 patients did not complete the treatment. The principle underlying treatment is the relaxation of hypertonic muscles by the powerful and prolonged contraction of the paralysed antagonists. In nearly all cases with contractures, which are the most suitable for this type of treatment, the flexor muscles are hypertonic and the current is therefore applied to the extensors. Return of voluntary movement keeps pace with relaxation of hypertonicity and is first noticed in the lower limb, although the upper extremity may alone have been treated. This surprising finding, together with the psychological improvement, which was out of all proportion to any objective benefit, suggests to the author that a central effect is involved. The possible mechanism of action is fully discussed.

The current used was of medium frequency and was occasionally faradic. With the latter, a frequency of at least 20 c.p.s. is required and some means of controlling the time of flow. Two small metal electrodes are placed on the patient's skin over pads saturated with saline and held firmly in place by rubber bands. Current is allowed to pass for 3 or 4 seconds and this is followed by a rest period of approximately 6 to 8 seconds. Treatment is

given daily and any one group of muscles should not be exercised for more than 5 minutes, that is, some 50 contractions a day. About 50 treatments are required. Intensity has to be controlled in order to avoid spread of the current to the flexor groups of muscles. In the upper extremity the current is applied to the triceps, the common extensor of the fingers, and the long extensor and abductor of the thumb; in the lower limbs maximal attention should be directed towards the peronei. Treatment of the hand is unsatisfactory owing to the marked tendency of the current to spread in that area. The intensity of the current varies from 10 to 300 mA., according to the muscle group being treated.

D. Preiskel

672. **Rehabilitation in Arthritic Diseases. A Two-year Follow-up**

J. P. GOFTON. *Annals of the Rheumatic Diseases* [*Ann. rheum. Dis.*] **16**, 456–459, Dec., 1957. 1 ref.

A statistical survey is reported of two years' working (1955 and 1956) of the British Columbia Division of the Canadian Arthritis and Rheumatism Society, which provides rehabilitation services to patients throughout this province. In the area served (approximately 600×800 miles; 966×1,288 km.) there are 20 individual treatment units, each staffed by a physiotherapist with adequate equipment; each unit is visited by a consultant twice a year. Nearly 4,000 patients were treated and 70,000 actual treatments given in each of the 2 years; some 2,500 cases were "closed" each year [but it is not clear whether this means discharged]. The majority of the patients were in the age group 49 to 64 years. In most cases the diagnosis came within the category of "rheumatism", although a few cases of poliomyelitis, cardiovascular disorders, and convalescence after operation were included, since the Society does not deny its facilities to any. The patients' condition before treatment and subsequent progress were assessed according to a "functional capacity code". The results in the year 1956 showed that 82·4% of patients over 64 were "improved" or "much improved", or had complete remission, the corresponding figures for the age groups 40 to 64 and under 40 being respectively 88·2% and 94·3%. At the end of 1956 approximately 90% of the patients had been under treatment for less than 2 years.

The author states that while "the inherent limitations in such a statistical survey are noted . . . the conclusion is drawn that the Society does much valuable work in preventing and alleviating disability and invalidism".

Harry Coke

673. **Rehabilitation of the Rheumatoid Cripple: a Five Year Study**

E. W. LOWMAN. *Arthritis and Rheumatism* [*Arthrit. and Rheum.*] **1**, 38–43, Feb., 1958.

The response of patients disabled by rheumatoid arthritis to an intensive programme of physical rehabilitation was studied by means of a 4-page list of activities concerned with the patient's everyday needs. By entering the date on which the patient became able to perform each activity independently, his physical capabilities at any moment could be accurately assessed and progress recorded. It was found that of 17 severely disabled patients whose average age was 46 and in whom the disease had been present for an average of 8 years, 6 were rendered completely self-sufficient and 5 of these retained their self-sufficiency throughout 3 years of follow-up. Of 21 less severely disabled whose average age was 40 and in whom the average duration of the disease was 8 years, 17 became totally self-sufficient and 12 of these remained so. Medical treatment was continued during the rehabilitation programme.

Of all the factors contributing to a successful result, the desire and willingness of the patient to take part in his or her own restoration was judged to be the most important. [This must be the experience of all who are engaged in this kind of work.] *G. S. Crockett*

674. **Underwater Exercises in the Treatment of Rheumatic Diseases and the Sequelae of Trauma.** (La kinébalnéothérapie des maladies rhumatismales et des séquelles traumatiques)

F. MAUVOISIN and J. BERNARD. *Annales de médicine physique* [*Ann. Méd. phys.*] **1**, 62–67, Jan.–March, 1958.

The authors describe the method of underwater treatment for patients with rheumatic diseases which has been in use at Aix-les-Bains for the last few years. The treatment must be carried out in a pool of adequate size and of a mean depth of 1·2 metre, and the temperature of the water should be maintained at 35° to 36° C.; the usual precautions are taken to prevent the spread of infection. Access to the pool may be gained by a non-slip ramp with suitable guard-rails. Another rail, placed around the periphery of the pool about 20 cm. below surface level, provides a hand-hold for patients doing exercises; wooden chairs (suitably counterweighted) can be suspended from this rail and the patient's trunk completely immersed. Patients are treated in groups of 10 or 12 under close supervision which, to be effective, requires the presence of the physiotherapist in the water. Exercises should not be continued for more than 20 minutes to avoid fatigue, which is lessened to some extent by rhythmic movements, and in any case they are followed by a compulsory rest period of one hour.

Among the conditions which are likely to benefit are "frozen shoulder", traumatic peri-arthritis of the shoulder, osteoarthritis of the hip, and lumbar disk lesions; for the latter condition exercises in flexion, which were once frowned upon, are of undoubted value in relieving muscle spasm and hastening rehabilitation.

D. Preiskel

675. **Rehabilitation in Rheumatic Diseases.** (La réadaptation dans les affections rhumatismales)

M. RUELLE and A. HENRARD. *Rhumatologie* [*Rhumatologie*] **10**, 55–65, March–April, 1958. 19 refs.

676. **The Treatment of Lumbago with Lumbar Exercises.** (Le traitement des lombalgies par la gymnastique lombaire)

G. SÉJOURNET. *Rhumatologie* [*Rhumatologie*] **10**, 98–101, March–April, 1958.

Neurology and Neurosurgery

677. **Activation with Megimide (β,β-Methyl-ethyl Glutarimide) in Electroencephalographic Investigations of Epileptic Conditions.** [In English]
S. Flodmark, I. Petersén, and K. Stenberg. *Acta psychiatrica et neurologica Scandinavica* [*Acta psychiat. scand.*] **33**, 69-82, 1958. 5 figs., 14 refs.

The authors draw attention to the advantages of using activating agents for use in electroencephalographic examination of epileptic patients, but point out the drawbacks of "metrazol", which has too low a convulsive threshold in normal subjects and which produces disagreeable side-effects. They have therefore investigated, at Sahlgrenska Sjukhuset, Göteborg, Sweden, the use of "megimide" (β,β-methylethyl glutarimide) for activation of the electroencephalogram (EEG) in a group of 58 patients, comprising 14 suffering from focal epilepsy, 17 from idiopathic epilepsy, 27 with suspected epilepsy, and 5 control subjects who showed no evidence of disease of the central nervous system and who had a normal resting EEG. The usual technique was that, 10 minutes after a conventional recording (including hyperventilation) had been made, a dose of 75 to 100 mg. of megimide was injected slowly intravenously. If a lower dose was found to have a powerful activating effect the injection was stopped.

In 33 cases (57%) there was definite accentuation of existing pathological activity noted in the resting record. In 15 cases (26%)—10 of these being in the group with suspected epilepsy—megimide gave rise to new activity, which was of epileptic type in 6 cases. Megimide produced little or no effect in the normal subjects in doses up to 100 mg. Subjective symptoms reported by the patients were limited to slight drowsiness, a feeling of tension, and occasional tingling in the finger-tips. The authors discuss the possible mechanism whereby the activating effect of megimide may be mediated. The significance of the findings is discussed, and the authors conclude that new abnormal activity appearing after administration of megimide constitutes evidence in favour of a diagnosis of epilepsy, provided that such activity is produced by very small doses of the drug.

J. B. Stanton

678. **Cerebrospinal Fluid Enzymes in Central Nervous System Lipidoses (with Particular Reference to Amaurotic Family Idiocy)**
S. M. Aronson, A. Saifer, G. Perle, and B. W. Volk. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. Soc. exp. Biol. (N.Y.)*] **97**, 331–334, Feb., 1958. 9 refs.

At the Jewish Chronic Disease Hospital, Brooklyn, New York, the levels of glutamic oxalacetic transaminase (G.O.T.), aldolase, and lactic dehydrogenase (L.D.) activity were assayed simultaneously in the serum and cerebrospinal fluid (C.S.F.) in 9 cases of infantile amaurotic family idiocy and 2 cases of Niemann–Pick disease, the estimations being repeated at varying stages of the illness. Similar enzyme studies were made as a control in 33 additional children with other neurological disorders.

In the patients with amaurotic idiocy the activity of G.O.T. and L.D. was invariably raised both in the serum and C.S.F., being highest during the earliest and most rapidly degenerative phase of the disease. In contrast to the findings of other workers, a distinct correlation was found between the activities in the serum and C.S.F., and it is suggested that when the increase of G.O.T. activity in the C.S.F. is sustained, as it is in the lipidoses, the postulated blood–brain barrier is overcome. In the patients with Niemann–Pick disease G.O.T. activity was high in both serum and C.S.F., but L.D. activity was raised only in the C.S.F. The activity of aldolase in the C.S.F. was raised in both diseases, but was normal or only transiently increased in the serum. In the control group a child with severe progressive cerebral disease of unknown aetiology was the only patient to show consistently high G.O.T. activity both in the C.S.F. and the serum, but 3 children with obstructive hydrocephalus had consistently high G.O.T. and aldolase activity in the C.S.F. with normal serum levels. The G.O.T. level was also raised in the C.S.F. in a case of craniopharyngioma.

In animal experiments a twofold rise in serum G.O.T. activity was noted in 10 dogs during 2 days subsequent to the injection of 1 g. of fresh heterologous canine grey matter (G.O.T. activity 80,000 units per g.) intramuscularly into each. No such rise occurred in 3 dogs injected with an inactivated cerebral homogenate. Since cerebral necrosis due to any cause liberates intracellular enzymes into the C.S.F., the authors suggest that neural degeneration in the lipidoses may be distinguished from that due to other disorders by the analysis of multiple enzymes in the serum and spinal fluid. *Celia Oakley*

679. **Dilantin in the Treatment of Trigeminal Neuralgia**
A. Iannone, A. B. Baker, and F. Morrell. *Neurology* [*Neurology (Minneap.)*] **8**, 126–128, Feb., 1958. 5 refs.

Reference is made to investigations on frog sciatic nerve in which it was found that the addition of "dilantin" (phenytoin) sodium to the bathing fluid reduced the excitability of a nerve which had been rendered hyperexcitable with sodium oxalate. The present authors have confirmed this finding and have carried out further experiments on mammalian nerve in which it was noted that the "nerve repetitions" or "rebound" spike induced by constant-current stimulation was abolished by the systemic administration of phenytoin sodium.

On the supposition that pain of peripheral nervous origin is related to repetitive discharge in the afferent fibre or end-organ an investigation of the effect of pheny-

toin sodium was therefore carried out on 4 patients with trigeminal neuralgia and one with glossopharyngeal neuralgia. The drug was given in doses of 0·1 g. or more 3 times a day. In all cases definite relief of pain was obtained and the paroxysms of pain were controlled. Relief was usually delayed for 24 hours after beginning the administration of the drug, and conversely recurrence of pain was delayed for 48 to 72 hours after its withdrawal.

The authors admit that the number of patients treated is too small and the period of observation too short for any definite conclusions to be drawn as to the efficacy of this treatment. *J. MacD. Holmes*

680. **Cervical Disk Lesions**

G. L. Odom, W. Finney, and B. Woodhall. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **166**, 23–28, Jan. 4, 1958. 12 refs.

In this paper from Duke University School of Medicine and Hospital, Durham, N. Carolina, are reviewed 246 cases of surgically verified cervical intervertebral disk lesions. These were causing either root or cord compression, and included both true protrusions composed of intervertebral disk tissue and bony spurs associated with degenerative changes in the cervical joints. Of the 221 lateral lesions with root involvement, 175 were disk protrusions and 46 bony spurs, the average age of patients in the former group being 43 and in the latter 49 years. Both types of lesion occurred at the interval between either the 5th and 6th or 6th and 7th cervical vertebrae in 90% of the cases. The symptomatology was of the now well recognized type. A motor defect was present in 204 (93%) of the 221 cases, and in lesions at the two common sites involved the triceps much more frequently than the biceps or deltoid. A sensory defect occurred in 173 (78%) of the cases, and at the periphery affected the thumb with 6th-root involvement (C5–6 protrusion) and the index finger with 7th-root involvement.

Radiological abnormalities in the cervical spine were present in three-quarters of the cases, but were of no value in location, corresponding to the myelographic abnormality in only 30% of the cases. Myelography gave valuable information in almost all the cases of disk protrusion, but revealed the level of a foraminal spur in only 18 out of 29 cases. The results of surgical treatment were considered excellent in 94 (57%) of the cases of disk protrusion and 19 (45%) of those of foraminal spur, all of the remaining patients having residual symptoms of greater or less severity. There were 5 re-operations for recurrent symptoms, and the only serious postoperative complication was due to cerebral anoxia occasioned by anaesthesia. There were no deaths in the series.

Of the 25 cases of medially placed lesions with cord compression, 14 had disk protrusion and 11 cervical spondylosis. The protrusions occurred at the three lowest cervical disks in patients whose average age was 46. Pain was rarely a feature, and the picture was one of a progressive spastic paraparesis with later involvement of the arms. Myelography revealed the lesion in each case and again indicated that the changes shown on plain films are misleading. The results of surgical removal were classed as good in 4 cases, satisfactory in 8, and poor in 2. In the cases of spondylosis the value of myelography was again apparent, and the results of surgery were classed as good or excellent in 2 cases, satisfactory in 6, and poor in 3. No attempt was made to excise either the lateral foraminal spurs or the transverse ridges in the cases of spondylosis with cord involvement.

[This is an excellent review of a large experience with cervical disk lesions. Although the authors consider that conservative treatment is indicated in the first instance, it is clear that only if the basis was quite markedly towards surgery could nearly 250 patients have had their cervical disk lesions surgically proved at one clinic in a 17-year period.] *J. E. A. O'Connell*

681. **Virus of Acute Encephalomyelitis of Man and Multiple Sclerosis**

G. W. A. Dick, F. McKeown, and D. C. Wilson. *British Medical Journal* [*Brit. med. J.*] **1**, 7–9, Jan. 4, 1958. 2 figs., 4 refs.

Some success has been claimed for the Russian " vaccine of Margulis and Shubladze " in the treatment of disseminated sclerosis. The vaccine is prepared at the Metchnikoff Institute, Kharkov, and in this paper from the Queen's University, Belfast, the authors summarize Soviet work on the virus, describing how the Russian workers (1) isolated what is known as the E.H.A. (*encéphalomyélite humaine aiguë*) virus from cases of sporadic encephalitis; (2) demonstrated it to be closely related immunologically to rabies virus; (3) found that sera from " a large percentage " of persons with disseminated sclerosis neutralized the virus; and (4) claimed amelioration of the disease in 30% of cases of disseminated sclerosis treated with a formolized vaccine prepared from the SV strain of the virus.

Before trying this vaccine in Northern Ireland the authors considered it desirable to find out more about the virus. They found the SV strain of E.H.A. virus to be infective for mice when injected by the intracerebral route, a widespread meningoencephalitis being demonstrable histologically by the 3rd day, with nerve-cell degeneration in the cerebral cortex and other sites and frank necrosis of cells, especially in Sommer's sector. Purkinje cells were also affected. Acidophilic inclusions of Negri-body type were readily demonstrated in the cytoplasm of nerve cells, these being best seen at a distance from the most intense inflammatory foci. The pathological changes in the spinal cord were similar but less marked. The authors conclude that the SV strain of the E.H.A. virus appears to be identical with the virus of rabies, and consider that the formolized vaccine prepared with it may possibly be dangerous in the treatment of patients with disseminated sclerosis.

In further tests samples of serum from 50 patients with disseminated sclerosis were examined for neutralizing antibody against antigens prepared with mouse brain infected with the SV strain; the virus–serum mixtures were inoculated intracerebrally into groups of mice.

None of the sera showed any significant neutralization of doses of 100 LD_{50} of virus. Occasionally there was survival of some of the mice given a dose of 10 LD_{50} of the virus–serum mixture, but this finding could not be regarded as evidence of specific neutralizing antibody, for similar results were found on occasion with sera from healthy human beings and rabbits. *Joyce Wright*

BRAIN AND MENINGES

682. **Clinical Significance of Impairment of Sound Localization**

L. P. Sanchez-Longo and F. M. Forster. *Neurology* [*Neurology (Minneap.)*] **8**, 119–125, Feb., 1958. 2 figs., 1 ref.

The ability to localize sound was investigated in 50 normal subjects by a method described previously by the authors, in which an ordinary eye perimeter is used with an audiometer earphone attached to its edge as the variable source of sound. The subject is blindfolded and placed in front of the perimeter with the ears equidistant from its edges. A difference in hearing of more than 20 db. between the two ears vitiates the test. In the subjects tested the accuracy of localization in both auditory fields was statistically the same, which probably indicates a lack of cerebral dominance in the function of hearing. Bilateral and symmetrical hearing loss for different frequencies did not impair localization to any significant extent.

The ability to localize sound was then studied in a series of 50 patients with cerebral lesions of different aetiologies and sites. It was found that patients with temporal-lobe lesions usually show impairment of sound localization in the contralateral auditory field.

It is suggested that this test may prove of value in the study of disease of the temporal lobe, but it cannot be used in patients who are confused or of poor intelligence. The presence of pronounced hearing defects and uncontrollable movements also make it impossible to carry out the test. *J. MacD. Holmes*

683. **Postnatal Development of the Arterial and Venous Networks in the Pia Mater of the Cerebral Hemispheres.** (Возрастные взаимоотношения артериальных и венозных сетей в мягкой мозговой оболочке больших полушарий головного мозга во внеутробной жизни)

E. V. Kapustina. *Педиатрия* [*Pediatrija*] **36**, 75–82, No. 2, Feb., 1958. 5 figs.

The development of the vascular network in the pia mater of the cerebral hemispheres is related to the development of the brain as a whole. The vascular network is differentiated earlier on the surface of the brain in those regions which morphologically and functionally mature early, as for instance the olfactory gyrus, but at a later period in those portions the development of which is slower, as for instance in the sincipital region. The differentiation of the arterial network takes place earlier than that of the venous network. In the process of development the venous network becomes less dense. This rarefaction of the network is the result of the reciprocal action of processes of development of all the components of the venous network, for instance, capillaries of the venous network develop into venules, venules into venous branches, and so on—in other words, the various venous components form shorter routes for the venous blood flow, thus ensuring a speedier cerebral circulation. *A. Orley*

684. **Lactic Dehydrogenase of Cerebrospinal Fluid in the Differential Diagnosis of Cerebrovascular Disease and Brain Tumor**

R. K. Jakoby and W. B. Jakoby. *Journal of Neurosurgery* [*J. Neurosurg.*] **15**, 45–51, Jan., 1958. 3 figs., 9 refs.

The differentiation between the signs due to cerebral vascular accident and those due to brain tumour frequently cannot be made with certainty, even after full investigation, including pneumoencephalography. In this preliminary report from the George Washington University Hospital, Washington, D.C., and the National Institutes of Health, Bethesda, the authors report the finding of a significant increase in lactic dehydrogenase (L.D.) activity in the cerebrospinal fluid (C.S.F.) after cerebrovascular accidents as compared with that in cases of brain tumour. Estimation of this enzyme is quick and simple. The authors employ a modification of the spectrophotometric assay method of Wroblewski and LaDue (*Proc. Soc. Exp. Biol. (N.Y.)*, 1955, **90**, 210) in which one unit of lactic dehydrogenase is regarded as the amount of enzyme per 0·3 ml. of C.S.F. causing a change in optical density at 340 mμ of 0·001 per minute, the results being designated by the symbol μ.

The average L.D. level in the spinal fluid of 20 patients whose final diagnosis was non-neurological was 10 μ, with a range of 2 to 18 μ. In 58 cases of cerebral conditions of various types, but excluding brain tumour, and 4 cases of meningitis the mean value was also 10 (range 2 to 20) μ. The mean L.D. value in the 4 cases of meningitis was 48 (range 32 to 65) μ, and was thus comparable with the values obtained in the cases of cerebral vascular accident reported below. In 17 cases of brain tumour the mean value was 14 (range 2 to 23) μ. This group included 4 cases of metastatic brain tumour with an average L.D. value of 15 μ. For comparison, in 18 patients who had suffered cerebral vascular accidents the average L.D. value was 31 μ (range 20 to 57 μ). It was noted that L.D. activity in the C.S.F. was generally higher in samples obtained several days after the stroke than in those examined soon after it.

The difference between L.D. activity in the C.S.F. after cerebral vascular accidents and all other samples of C.S.F. tested was statistically significant ($P<0·001$), but the authors point out that their study was based on cases requiring admission to hospital and that the L.D. values after "little strokes" may not be so high. However, they conclude that the test should prove useful in the differential diagnosis of cerebral vascular disease from brain tumour.

[Other workers have reported high L.D. activity in the C.S.F. in the presence of secondary, but not of primary cerebral tumours.] *Celia Oakley*

685. **Anticoagulant Therapy in Cerebral Vascular Disease —Current Status**

C. H. MILLIKAN, R. G. SIEKERT, and J. P. WHISNANT. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **166**, 587–592, Feb. 8, 1958. 12 refs.

This report from the Mayo Clinic is concerned with the effect of anticoagulant therapy on 4 meticulously selected syndromes of cerebrovascular disorder [and not with cerebral vascular disease in general: the title is therefore somewhat misleading]. The authors lay great emphasis on the " absolute importance ", in attempting to evaluate the effect of anticoagulant therapy in cerebrovascular disease, of knowing what type of stroke is being dealt with. They describe the diagnostic criteria whereby their 317 patients were selected and separated into the following 4 groups (citing single case-histories illustrative of each group): (1) 94 patients with " intermittent insufficiency in the vertebral–basilar system "; (2) 85 patients with " intermittent insufficiency in the internal carotid arterial system "; (3) 107 cases of infarction (" irreversible thrombosis ") in the distribution of the vertebral–basilar system; and (4) 31 cases of actively advancing thrombosis in the internal carotid arterial system (" slow stroke "; " stroke in evolution "). All these patients were given anticoagulant drugs. Heparin (50 mg. 4-hourly) was given intravenously when rapid action was desired; and a single dose of ethyl biscoumacetate was given by mouth together with the first dose of bishydroxycoumarin, with which oral treatment was then continued, the dose being adjusted from day to day to maintain the prothrombin time between 35 and 40 seconds (18 to 20 seconds being regarded as normal).

In 90 of the 94 patients in Group 1 the attacks ceased completely when effective anticoagulant therapy had been established. In the remaining 4 patients the attacks diminished in frequency and severity; none progressed to thrombosis and infarction within the vertebral–basilar system. Of the 85 patients in Group 2, 82 were completely relieved of symptoms. The attacks continued in 2 patients, but with diminished frequency and severity, and only one developed carotid arterial occlusion with hemiparesis. Of the 107 patients in Group 3, 9 (8%) died, in contrast to a mortality of 18 (58%) out of 31 similar cases (not included in this series) which were not treated with anticoagulants. There was no advance in the neurological deficit in 29 of the 31 patients in Group 4. Only 2 (6%) developed complete hemiplegia, compared with 5 (35%) who became hemiplegic out of 17 similar patients (not included in this series) who did not receive anticoagulants.

The authors enjoin that " the administration of anticoagulants [in cerebral vascular disorders] should be sharply limited to patients in whom the type of cerebrovascular disease has been meticulously defined ". They indicate that they are engaged in following up a series of untreated patients to act as controls for the first two groups described in the present paper and state that " much more extensive study [of cases within Groups 3 and 4] is needed before final conclusions are made ". Nevertheless they are firmly of opinion that anticoagulants exert a significantly favourable effect in cases of intermittent cerebral vascular insufficiency as defined for Groups 1 and 2, and affirm " a definite clinical impression " that anticoagulant therapy is also of benefit in the entities defined for Groups 3 and 4.

[Although much important information is omitted—in particular, the duration of observation of patients both on treatment and subsequently—the authors' conclusions command respect for their sober caution and strict circumspection.] *P. D. Bedford*

686. **Present Status of Anticoagulant Treatment of Cerebral Vascular Lesions**

E. MCDEVITT, I. S. WRIGHT, and W. T. FOLEY. *Medical Clinics of North America* [*Med. Clin. N. Amer.*] 42, 587–601, May, 1958. 2 figs., 23 refs.

687. **ACTH and Adrenal Steroids in the Treatment of Pneumococcal Meningitis in Adults**

J. C. RIBBLE and A. I. BRAUDE. *American Journal of Medicine* [*Amer. J. Med.*] **24**, 68–79, Jan., 1958. 41 refs.

This paper from the University of Texas Southwestern Medical School, Dallas, records 12 consecutive cases of pneumococcal meningitis occurring in adults aged 27 to 73 which were treated with penicillin, ACTH (corticotrophin), and corticosteroids given concurrently and resulted in only one death.

The treatment of pneumococcal meningitis has been uniformly less successful in adults than in children despite the use of antibiotics which are known to sterilize the cerebrospinal fluid (C.S.F.), suggesting that the failure of treatment may be due to factors other than the persistence of living pneumococci. In the present series 20 to 60 mega units of penicillin was given by intravenous infusion daily for one to 3 weeks, part of the dose being given intramuscularly in some cases, and 40 to 160 units of ACTH, with or without 100 to 200 mg. of cortisone or hydrocortisone, was given daily, with the penicillin or intramuscularly, for 3 to 9 days. The pressure and protein content of the C.S.F. fell promptly, with a concurrent clinical improvement.

The recovery rate of 92% in this small series is higher than any previously reported among adults treated without adrenal steroids, and there was no objective residual neurological damage in the survivors. The authors observe that their results indicate these hormones may be given to desperately ill patients (9 of their 12 were comatose on admission) without any untoward effects on their resistance to infection. The rationale of steroid therapy in pneumococcal meningitis is discussed. Massive exudation may act mechanically to increase morbidity as well as impairing the bactericidal action of penicillin by causing bacteriostasis and by protecting intracellular pneumococci from contact with the drug. In addition to their anti-inflammatory effect the steroids may suppress the allergic response to pneumococcal nucleoprotein; this hypersensitivity increases the amount of exudate and thus prolongs the meningitic illness in the absence of persisting live pneumococci.

Case histories and full details of treatment are given, and there is a review of the relevant literature.

Celia Oakley

Psychiatry

688. **A Case of Diabetes Mellitus. A Study of Psychosomatic Medicine**
A. K. RAYCHAUDHURY. *Psychosomatic Medicine* [*Psychosom. Med.*] **20**, 33–41, Jan.–Feb., 1958.

In this paper from the Government College of Physical Education, Narkeldanga, West Bengal, a clinical psychosomatic study of a 54-year-old male Hindu suffering from diabetes mellitus is reported. The diabetic symptomatology was first apparent shortly after the patient had a severe emotional upheaval when, during the riots of 1950, he was forced to leave Pakistan for India, where he felt unwelcome and acutely anxious.

In this case predisposition to the illness is recognized in a family history of diabetes mellitus, increasing obesity before the onset of the illness, and, possibly, the life-long consumption of a high-rice diet. The psychosocial background of the patient is also considered to have increased proclivity to the disease. In infancy there was inhibition of feeding because the patient's elder brother continued to feed at the mother's breast at the same time, and in adult life he suffered from functional dyspepsia. Masochistic and obsessional traits were pronounced. Hinduism is in itself a religion of earthly suffering and personal purification, and in this particular case the situation was complicated by the fact that the patient's early life was dominated by the religio-cultural clashes of Hinduism, Islam, and Christianity. His associated aggressive feelings did not reach verbal or motor expression; instead, they were directed against himself.

The author suggests that unconscious guilt feelings and a need for punishment, which induced a strong masochistic drive in the patient, were satisfied through the disease and, incidentally, through its method of treatment.

A. Balfour Sclare

689. **Guide to Psychosomatic Literature in Germany since 1945**
M. PFLANZ and T. V. UEXKÜLL. *Journal of Psychosomatic Research* [*J. psychosom. Res.*] **3**, 56–71, 1958. Bibliography.

690. **Psychoanalytic Contributions to Psychosomatic Research**
L. LINN. *Psychosomatic Medicine* [*Psychosom. Med.*] **20**, 88–98, March–April, 1958. Bibliography.

A critical review of the significant contributions made by psychoanalysis to contemporary methodology in psychosomatic research is presented in this paper from the Mount Sinai Hospital, New York. The elucidation of unconscious conflicts stemming from aggressive or libidinal drives is considered by the author to be of practical as well as theoretical value; anorexia nervosa is cited as an example of a psychosomatic disorder in which a detailed understanding of psychodynamics is of pragmatic value in treatment. There is an increasing body of evidence from the field of experimental psychosomatic studies that unconscious processes in both subject and experimenter may constitute important variables. The study of a patient with a gastric fistula reported by Margolin (*J. Mt Sinai Hosp.*, 1953, **20**, 194) indicated that experimental results could be powerfully influenced by the transference relationship with the experimenter and by phantasies connected with the experimental techniques employed. Emotional changes in the experimenter himself may also be a significant variable in laboratory investigations.

Some of the advantages and limitations of psychoanalysis as a research tool in psychosomatic medicine are discussed. During psychoanalytic sessions, for instance, the occurrence of vegetative symptoms may sometimes be fruitfully studied *in statu nascendi*. A considerable methodological difficulty, however, may arise when the subject attempts to reconcile his role as a patient with his role as a research collaborator. The need to establish "bridges of communication" between psychoanalysis and neurophysiology is pointed out. Similarly, an effort should be made to find a common language between psychoanalysis and modern ethology.

A. Balfour Sclare

691. **Assessment of the Results of Treatment with Casein Hydrolysate Poor in Phenylalanine in Phenylpyruvic Oligophrenia.** (Erfolgsbeurteilung der diätetischen Behandlung mit phenylalaninarmem Caseinhydrolysat bei der Oligophrenia phenylpyruvica)
R. GRÜTTNER, F. MÜLLER, and H. WALLIS. *Monatsschrift für Kinderheilkunde* [*Mschr. Kinderheilk.*] **106**, 41–45, Feb., 1958. 3 figs., 22 refs.

At the University Paediatric Clinic, Hamburg–Eppendorf, 3 children, aged 1¼, 2¼, and 3¼ years respectively, who were suffering from phenylpyruvic oligophrenia were given for several months a diet poor in phenylalanine, the authors' aim being to ascertain whether this expensive form of dietetic treatment was justified by its beneficial effect on intellectual function and motor development. As a source of protein the diet contained a casein hydrolysate enriched with tyrosine and tryptophan, of which each child received 2 to 2·5 g. per kg. body weight daily. Fat was given in the form of coconut margarine and olive oil (3 g. per kg. body weight daily), and carbohydrate as glucose and wheat starch (10 g. per kg. daily). The diet also contained necessary minerals and salt (in the form described by Woolf *et al.* (*Brit. med. J.*, 1955, **1**, 57; *Abstr. Wld Med.*, 1955, **18**, 155)), together with vitamins and free fluid. After a few weeks the diet was supplemented by 150 to 300 ml. of milk daily, root vegetables, and fruit.

In one child the serum protein level sank so low that marked oedema developed. This condition improved, however, after addition of milk to the diet. The intellectual and motor function of the children under treatment improved, but only to a very limited extent, and the

children remained on the level of idiots. The authors conclude that to be effective this type of dietary treatment should be instituted in the first few months of life, before irreparable damage to the brain has developed.

F. K. Taylor

692. **The Prognostic Value of the Clinical Picture and the Therapeutic Value of Physical Treatment in Schizophreniform States.** [In English]

L. EITINGER, C. L. LAANE, and G. LANGFELDT. *Acta psychiatrica et neurologica Scandinavica* [*Acta psychiat. scand.*] **33**, 33–53, 1958. 16 refs.

The starting point of this investigation was the division of schizophrenia into true schizophrenia and schizophreniform psychosis proposed by Langfeldt in 1937 on the ground that an accurate diagnosis will affect the treatment and prognosis. The various interpretations placed by different authors on the term "schizophrenia" are discussed. The investigation consisted in a follow-up review by the two junior authors during 1955–6 of 154 patients (out of 783) who were admitted to the University Psychiatric Clinic, Vinderen, Oslo, during the period 1940–9 and who had been discharged with a diagnosis of either schizophrenia or schizophreniform psychosis. At the same time and quite independently the case histories of these patients were reviewed by the senior author (Langfeldt), who gave a diagnosis and prognosis in each case based on the actual symptomatology presented by the patient at the onset of the disorder. On this basis Langfeldt divided the 154 cases into 110 cases of true schizophrenia and 44 of schizophreniform psychosis. As a result of the follow-up study it was considered that of the 110 cases, 105 were indeed cases of true schizophrenia, but that 5 were cases of schizophreniform psychosis. Of the 44 cases assessed by Langfeldt as schizophreniform, 39 were confirmed at follow-up and 5 were found to be cases of schizophrenia. There was thus a notable agreement between the diagnosis based on symptomatology at the time of initial admission and the findings at follow-up examination.

The authors also discuss the possible effects of physical treatment on the expected course and prognosis of patients in these two groups. Of the schizophrenic patients, 85 had received somatic treatment, including electric convulsion therapy, insulin coma therapy, and lobotomy, but the results in this group were extremely poor, only 5% becoming capable of living a socially independent life, the rest being either returned to hospital or receiving public care in some other form. Of the 44 schizophreniform patients, 33 were given somatic treatment as above and a comparatively good result was obtained in about three-quarters of them. Failure in prognosis was mainly due to the admixture of other psycho-pathological conditions, such as cases of organic brain disorder or mental deficiency. Since the physical methods of treatment employed in the schizophreniform group were the same as those used for the schizophrenics, such treatment may therefore be considered to be effective in the schizophreniform psychoses, although completely inadequate for patients with true schizophrenia. (The authors admit, however, that an untreated control group was not available.) They conclude that patients admitted to hospital with a diagnosis of "schizophrenia" can be divided into two groups in the manner described above, and that in all probability these groups represent different forms of the disorder in respect both of symptomatology and of prognosis.

J. B. Stanton

693. **Treatment of the Chronic Paranoid Schizophrenic Patient**

D. E. CAMERON and S. K. PANDE. *Canadian Medical Association Journal* [*Canad. med. Ass. J.*] **78**, 92–96, Jan. 15, 1958. 4 refs.

The authors present, from McGill University, Montreal, a method of treatment of chronic paranoid schizophrenia which they claim has been more successful than any previously reported. This consists in a combination of prolonged sleep and electric shock therapy. Three barbiturates and chlorpromazine ("largactil") are used to produce the sleeping state. The patient sleeps 20 to 22 hours daily, being wakened only for food and toilet. Electric shock therapy is instituted after 10 days. The aim is to produce confusion to a degree described as "complete depatterning"; the patient loses all spatial and temporal image to the point of not being aware of the loss. This stage is reached between the 30th and 60th days of sleep and after about 30 shock treatments. It is maintained for 5 to 7 days, after which shocks are reduced to 3 weekly and the medication is gradually tapered off. Rehabilitation begins after 4 or 5 days and lasts about one month. Any sign of delusional thinking is treated by intensification of shock treatment. Patients receive a thorough examination both before and after treatment, and are followed up for 2 years. During the follow-up period shock therapy is continued monthly, psychotherapy being limited to support and guidance from a strong personal relationship.

The effect of this treatment was studied in 26 patients, 16 of whom had had symptoms for more than 2 years. Of the 16 chronic patients, all except one showed good initial response. This patient left hospital against advice and has since been readmitted for further treatment. Two patients developed paranoid fixations during the follow-up period and refused to continue, but their readmission to hospital was not considered necessary. Three others had to be readmitted for further treatment; one of these is still under treatment, but the other 2 are now doing well. With the exception of the 2 patients who refused follow-up care and the one still being treated, none shows any symptoms of paranoia, although some schizophrenic damage, such as blunting of affect and loss of drive, is present. All 10 patients who had been ill less than 2 years responded well, and evidence of permanent schizophrenic damage is rare. There were minor relapses in both groups, which were satisfactorily treated without admitting the patients to hospital.

E. H. Johnson

694. **Biochemical Aspects of Schizophrenia.** [Review Article]

H. HOAGLAND. *Journal of Nervous and Mental Disease* [*J. nerv. ment. Dis.*] **126**, 211–220, March, 1958. 24 refs.

Dermatology

695. **The Mental Action and Antihistaminic Efficacy of Phenyltoloxamine in Cutaneous Disorders**
R. FLEISCHMAJER, S. BLAU, and N. B. KANOF. *Antibiotic Medicine and Clinical Therapy* [*Antibiot. Med.*] **5**, 120–124, Feb., 1958. 6 refs.

Phenyltoloxamine was tried in the management of 50 dermatological patients, 35 of whom were suffering from pruritic dermatoses and all had severe tension, insomnia, and anxiety. The dosage was 500 mg. daily for 1 to 8 weeks. In all, 42 patients experienced definite relaxation, tranquillization, and relief of insomnia, and of the 35 patients with pruritus, 31 obtained complete or substantial relief from irritation, this being attributed to the potent antihistaminic properties of phenyltoloxamine.

Although the drug is an effective ataraxic, side-effects occurred in most cases, including drowsiness, blurred vision, vomiting, and " marked hypnosis ". In 3 cases treatment had to be discontinued because of severe reactions, manifested by nausea and marked drowsiness in 2 cases and by tachycardia and dryness of the oral mucosa in the third. The side-effects were reduced to a minimum when the daily dose was lowered to 300 mg.

R. R. Willcox

696. **The Allergic Origin of Zirconium Deodorant Granulomas**
W. B. SHELLEY and H. J. HURLEY. *British Journal of Dermatology* [*Brit. J. Derm.*] **70**, 75–101, March, 1958. 5 figs., bibliography.

The authors present, from the University of Pennsylvania School of Medicine, Philadelphia, the results of an extensive study of the recently recognized type of axillary granuloma associated with the use of zirconium (Zr) deodorants. The literature (based on 64 cases) is reviewed and 6 further cases are added. The several theories regarding the causation of this condition have included (1) foreign-body reaction to the metal Zr or to some other component of the deodorant stick, (2) secondary reaction to apocrine sweat extravasation, and (3) some form of allergic mechanism, but none of these possibilities has been further investigated. The fact that the appearance of the axillary granuloma coincided with the introduction of new deodorants containing sodium zirconium lactate and that the majority of the patients reported (predominantly women) had used such a deodorant suggested that Zr was the most likely compound implicated in the causation of the granuloma.

A test was therefore arranged in which 30 healthy males applied a commercial deodorant containing Zr to one axilla each morning and a Zr-free deodorant, which was otherwise identical in composition with the zirconium stick, to the other. After a month one of the men developed a chronic granulomatous condition in the axilla treated with the Zr stick which was clinically and histologically identical with those seen occurring in patients seen previously. In a further test the men applied different concentrations of Zr in a plain sodium stearate soap vehicle; again one man, not the same subject, developed a granulomatous response. All the test subjects gave a negative result to patch tests with the Zr deodorant; however, intradermal testing with sodium zirconium lactate demonstrated that the 2 men who had previously reacted to the Zr deodorant developed a unique granulomatous response while the rest were unaffected. In these 2 subjects it was possible by serial dilution tests to elicit a response when the Zr was present in a concentration of only 1 in 1,000 to 1 in 10,000.

These experimental findings were then checked in 4 patients who had developed the eruption clinically. Once again the patch test with Zr gave a negative result but the intradermal test with Zr in a concentration of 1 in 1,000 to 1 in 10,000 gave a granulomatous response in all 4 patients. As the authors point out, the finding that trace amounts of a simple metallic ion may produce a granuloma introduces a new aetiological concept into the pathogenesis of disease. The mechanism of action is considered to be allergic in nature. *G. W. Csonka*

697. **Pyoderma Gangrenosum with an Unusual Syndrome of Ulcers, Vesicles, and Arthritis**
S. AYRES, Jr. and S. AYRES III. *A.M.A. Archives of Dermatology* [*A.M.A. Arch. Derm.*] **77**, 269–280, March, 1958. 9 figs., 13 refs.

The authors review the literature of pyoderma gangrenosum and then describe the clinical and histological findings in 4 patients (2 male, 2 female) aged between 47 and 61 who came under their care because of long-standing, chronic, recurrent, spreading ulcers on the limbs and trunk with the typical raised purplish borders and erythematous halo. All the patients had severe chronic arthritis, which was of the rheumatoid type in 3, but none showed evidence of any other debilitating disease and none had ulcerative colitis. In 3 patients crops of vesicles developed while under observation, and in 2 of these the eruption resembled that of dermatitis herpetiformis; in the third patient there were only a few nondescript haemorrhagic vesicles.

Because the vascular eruption resembled that of dermatitis herpetiformis treatment with sulphonamides was instituted; all 4 patients obtained marked benefit, but were not cured, following administration of sulphapyridine. Improvement was noted particularly in the vesicular lesions and the ulcers, but in only one case was there any improvement in the arthritis. The authors consider, as do other workers, that pyoderma gangrenosum is not primarily a local condition and is not necessarily dependent on some underlying debilitating disease such as ulcerative colitis.

[No search was made in these cases for lupus erythematosus cells.] *Benjamin Schwartz*

Paediatrics

698. **A Consideration of Colostrum and Milk as Sources of Antibodies Which May Be Transferred to the Newborn Baby**

K. E. BOORMAN, B. E. DODD, and M. GUNTHER. *Archives of Disease in Childhood* [*Arch. Dis. Childh.*] **33**, 24–29, Feb., 1958. 4 figs., 9 refs.

The authors estimated the titres of anti-A and anti-B agglutinins in samples of serum, colostrum, and milk from 97 mothers and compared these with the titres in samples of the infants' serum taken at birth and 3 and 10 days post partum. Some correlation was noted between the titres in maternal serum and in colostrum and milk, but none between colostrum or milk titres and those of the infants' serum. When milk or serum containing Rh antibodies was given by mouth to one Rh-positive and 20 Rh-negative infants there was no evidence of their being absorbed. However, since the sensitivity of the methods used was insufficient to exclude the possible absorption of traces of antibody, expression and boiling of breast milk are advocated in the feeding of infants with haemolytic disease during the first week of life. *Wilfrid Gaisford*

699. **Studies of Respiratory Insufficiency in Newborn Infants. III. Respiratory Rates and Birth Weights of Premature Infants as Guides to Their Survival and Need for Oxygen Therapy**

H. C. MILLER. *Pediatrics* [*Pediatrics*] **20**, 817–826, Nov., 1957. 11 refs.

Changes in the respiratory rate and the incidence of apnoea and bradypnoea were noted during the first week of life in premature infants born at the University of Kansas Medical Center, Kansas City, from August, 1954, to December, 1956, and the findings studied in relation to the survival of the infants and their need for oxygen. All babies weighing between 1,001 and 2,500 g. at birth were included, 88% being negroes. The 350 babies were divided into three groups: (I) 126 whose respiration rate was considered to be normal (about 40 per minute) during the first hour and showed no great increase or decrease subsequently; (II) 122 whose respiration was comparatively rapid in the first hour but fell to normal rates subsequently; and (III) 102 babies who had a low, normal, or high mean respiration rate during the first hour and showed a significant increase (that is, an increase of 15 or more per minute) in the rate at some time during the first 2 days. "Initial apnoea" is defined as "a delay of more than 2 minutes in the onset of sustained, spontaneous respirations", even if preceded by occasional gasping, and "late apnoea" as "a cessation of respiration lasting more than 60 seconds, after sustained, spontaneous respirations become established". The term "initial bradypnoea" is used to indicate that a respiration rate of 40 per minute or more was not recorded during the first hour and "late bradypnoea" to indicate a respiration rate of less than 20 per minute recorded more than one hour after the infant's birth.

No deaths occurred among the 248 babies in Groups I and II during the first week of life, 2 of whom (one in each group) received oxygen therapy (that is, they were treated for more than one hour continuously with 40% oxygen). Of the 102 babies in Group III, however, 61 received oxygen therapy and 23 died. The mortality among the 285 babies of all groups weighing more than 1,750 g. at birth was less than 2%, whereas 25% of the 61 whose birth weight was less than 1,750 g. died. About 20% of those with the higher birth weight and about 80% of those with the lower birth weight were in Group III, the mortality among infants of low birth weight in this group being significantly higher than among those of higher birth weight ($P<0.02$). The incidence of early and late apnoea and bradypnoea was significantly less among the heavier infants, and when they did occur they were associated with a negligible mortality. Initial apnoea, which was not significantly associated with a low birth weight, occurred in 19 babies, of whom 11 died. On the other hand the incidence of initial bradypnoea was highest in babies with a birth weight below 1,250 g. Of 11 babies whose respiration rate was below 40 per minute in the first hour, 7 died, while of 50 babies whose respiration rate exceeded 40 per minute in the first hour, only 8 died. There were 9 deaths among the 14 babies with late bradypnoea, who were not predominantly of low birth weight, though all were in Group III.

The author concludes that oxygen therapy need not be given to premature babies who are acyanotic within a few minutes of birth, in whom sustained, spontaneous respiration is established within 2 minutes of birth, and whose respiration rate reaches 40 per minute or more within the first hour, with no significant subsequent increase. He suggests that careful records should be kept of the respiration rate of all infants weighing less than 1,750 g. at birth.

[These findings can do no more than confirm the clinical impressions of all those experienced in the care of premature babies.] *Pamela Aylett*

700. **Stosstherapy in Acute Respiratory Infection in Children**

M. C. JOSEPH. *British Medical Journal* [*Brit. med. J.*] **1**, 487–493, March 1, 1958. 13 figs., 22 refs.

"Stosstherapy" or "shock dose" is the term used to describe the treatment of pneumonia or other infections by a single massive dose of an antibiotic. The object of the present study was to compare the results of such therapy with those of standard continuous therapy in acute lower respiratory infection in children, patients at the Evelina Children's Hospital of Guy's Hospital, London.

Of 52 children given stosstherapy, 48 received both sulphadimidine and penicillin and 4 penicillin alone. The sulphadimidine was given by mouth in a dose of 0·3 g. per kg. body weight (maximum 4 g.), and the penicillin by intramuscular injection in a dose of 0·2 to 0·5 mega unit. In the " standard " group (54 children) treatment was with repeated intramuscular injections of penicillin either alone or accompanied by oral administration of sulphadimidine and was usually continued for at least 5 days. The response in both groups was judged on careful analysis of temperature and of pulse and respiration rates; appropriate graphs are presented to illustrate these points. Other studies covered physical signs in the chest, clearing of radiographs, length of stay in hospital, and secondary fever.

Results were judged to be successful in 43 of the 52 patients given stosstherapy and 46 of the 54 treated by standard methods; complications occurred in 3 and 4 cases in the two groups respectively. The absence of side-effects of stosstherapy is particularly noted and the advantages of the treatment are emphasized—namely, only one injection has to be given, the child's rest and sleep are not disturbed, time and labour are saved, and patients are able to enjoy their food sooner. An additional advantage is the saving in cost; at the time of the investigation (1952–4) stosstherapy for 50 patients cost about £3 10s., compared with £18 10s. for standard treatment. Because it has these advantages over standard treatment as well as giving equally good results the author suggests that stosstherapy should be the method of choice for the treatment of acute infections of the lower respiratory tract in children. *J. M. Smellie*

701. **Etiological Factors in Cerebral Palsy and Their Correlation with Various Clinical Entities**

S. BRANDT and V. WESTERGAARD-NIELSEN. *Danish Medical Bulletin* [*Dan. med. Bull.*] **5**, 47–52, Feb., 1958. 10 figs., 6 refs.

An investigation of the cause of cerebral palsy among Danish children seen in clinics at orthopaedic hospitals in Aarhus and Copenhagen is described. The disease was acquired in the prenatal or paranatal period in 87% of 628 cases and in the postnatal period in only 13%. Prenatal factors (36% of the total), including prematurity, accounted for 54% of cases of symmetric diplegia and paraplegia and 41% of those of asymmetric diplegia. Paranatal factors (31% of the total) were the most common cause of athetosis. Single factors of importance were prematurity (27%) and neonatal asphyxia (23%). Prematurity appeared to be 3 to 4 times more frequent a cause of symmetrical spastic diplegia and paraplegia than of extrapyramidal hyperkinesia; in contrast, neonatal asphyxia was 3½ times more frequent in extrapyramidal hyperkinesia than in spastic diplegia. The risk of severe mental defect and motor dysfunction was greater in children with a history of neonatal asphyxia than in those with a history of prematurity only. Rh incompatibility was observed in only two clinical subgroups—spastic paraplegia (1 out of 81 cases) and extrapyramidal hyperkinesia (10 out of 84 cases). Multiple births were 4 times more frequent in the groups with spastic diplegia and tetraplegia than in normal subjects. None of the children in the series was delivered by caesarean section. Genetic factors controlling the inheritance of neurological disease probably accounted for less than 4% of the 628 cases. The authors suggest that improved obstetric technique, by lessening the incidence of prematurity, neonatal asphyxia, and Rh incompatibility, might lead to a reduction in the number of cases of cerebral palsy. *William Hughes*

702. **Conversion Hysteria in Childhood**

A. HINMAN. *A.M.A. Journal of Diseases of Children* [*A.M.A. J. Dis. Child.*] **95**, 42–45, Jan., 1958. 11 refs.

The author reports that during a period of 10½ years 28 children (21 girls and 7 boys aged 4½ to 14 (median 11) years) were admitted to the paediatric service of the North Carolina Baptist Hospital, Winston-Salem, with a diagnosis of conversion hysteria, the total paediatric admissions during this period being 10,935 cases. It is suggested that this somewhat higher than expected incidence may be associated with the isolated, economically backward, and culturally infantile nature of the population of the district. The symptomatology was wide, but a table of the commoner manifestations shows that these included somatic manifestations, episodal performances, fugues, paralogia, and multiple personality. Hysteria in childhood may simulate organic disease and may even lead to organic changes such as atrophy and contractures. Usually, however, the symptoms are bizarre and dramatic and are absent during sleep.

It is stressed that the conversion, which is the result of deep emotional conflict, is an end in itself and thus the patient is unconcerned about the symptoms, even when these are crippling. This is in marked contrast to the hypochondriac or the malingerer, both of whom take a marked interest in their symptoms. The hysterical child is immature, needs to be the centre of attention, undergoes swings of mood and extremes of emotional expression, is suggestible, and is usually happy and unaware of conflict. The development of normal emotional ties with the parents is often difficult. Two illustrative case histories are given. The first child, a girl aged 11, developed convulsions after a third exacerbation of acute nephritis. Ether anaesthesia was required to control them, sedatives and anticonvulsants having no effect. She also refused to eat, and intravenous feeding was used. The second child, a girl aged 9, developed paralytic symptoms after an attack of varicella, and complained of severe abdominal pain, but complete physical examination revealed no cause. These cases should be dealt with by calm, firm handling and psychotherapy. The non-dramatic approach helps in the reconversion of symptoms which, it is stressed, is a necessary preliminary to psychotherapy.

E. H. Johnson

703. **Convulsions in Childhood.** [Review Article, in English]

H. ZELLWEGER. *Annales paediatrici* [*Ann. paediat. (Basel)*] **190**, 257–277, May, 1958. 1 fig., 22 refs.

Medical Genetics

704. **The Genetic Mechanism of Idiopathic Hyperlipemia**
J. D. Boggs, D. Yi-Yung Hsia, R. F. Mais, and J. A. Bigler. *New England Journal of Medicine* [*New Engl. J. Med.*] **257**, 1101–1108, Dec. 5, 1957. 6 figs., 49 refs.

From the Children's Memorial Hospital (Northwestern University Medical School), Chicago, the authors describe a Puerto Rican family in which 3 of the children suffered from idiopathic hyperlipaemia. At necropsy on one of these children, a girl aged 10, marked atherosclerosis of the endocardium and of the large and medium-sized arteries was found, together with coronary arterial occlusion and myocardial infarction. The parents of the children, who were first cousins, were apparently free from symptoms. However, both parents and also one asymptomatic sib of the affected children showed increased levels of total plasma lipids and of both total and esterified cholesterol. It is suggested that the patients were homozygous for a rare abnormal gene which, in heterozygotes, produces a minor defect in lipid metabolism in the absence of clinical symptoms. The findings in similar previous family studies reported in the literature are reviewed and shown to be consistent with this hypothesis.

H. Harris

705. **Hemostatic Data in Relatives of Hemophiliacs A and B. Evidence for Modifying the Classical Sex-linked Recessive Hypothesis**
P. Didisheim, J. H. Ferguson, and J. H. Lewis. *A.M.A. Archives of Internal Medicine* [*A.M.A. Arch. intern. Med.*] **101**, 347–354, Feb., 1958. 8 figs., 40 refs.

From the Universities of Pittsburgh and North Carolina the authors report a study of 77 females who were "obligatory carriers" of haemophilia (haemophilia A) or Christmas disease (haemophilia B). An obligatory carrier was so defined as to exclude the mothers of a single haemophilic child in whom the disease might have arisen by gene mutation. The tests used included determination of: (1) the blood clotting time both in glass and siliconized glass; (2) the prothrombin consumption time after both 1-hour and 2-hour incubation of the serum; and (3) assays for deficiency of both the anti-haemophilic globulin factor (A.H.F.) and the Christmas factor (P.T.C.). In addition, the thromboplastin generation test was employed to assay the two factors. All these examinations were carried out a second time one year later, and there was striking agreement between the results obtained.

By the most sensitive of the tests, that is, the specific factor assays, 19·8% of the carriers showed some haemorrhagic abnormality. The other tests were less sensitive, the least so being the blood clotting time in glass, which gave a positive result in only one instance. A history of haemorrhagic phenomena thought to be in excess of normal bleeding was given by 28% of the carriers, but of those who showed some abnormality in one or more of the laboratory tests, 52% had such a history, compared with 20% of those with normal test results.

These findings are discussed in relation to the sensitivity of the tests employed and to their genetic implications. It is suggested that the occurrence of the genes for haemophilia or Christmas disease by mutation must be exceedingly rare. Thus the mother of a single haemophilic son or female carrier is probably genetically identical with an obligatory carrier, a family history of the disease being either forgotten or denied. Furthermore, it is concluded that the genes for haemophilia and Christmas disease are not completely sex-linked recessive and that partial expression may occur, as in the carriers with the abnormalities described in this study.

A. G. Baikie

706. **Unusual Transmission of the Haemophilic Gene**
J. F. Wilkinson, M. C. G. Israëls, F. Nour-Eldin, and R. L. Turner. *British Medical Journal* [*Brit. med. J.*] **2**, 1528–1529, Dec. 28, 1957. 1 fig., 19 refs.

The authors report a family in which haemophilia has occurred in 5 generations in conformity with the expected pattern for sex-linked recessive inheritance. In Generation V, however, there are 2 affected female offspring of a first-cousin marriage; each of these has married outside the family and each has one affected daughter. Full laboratory investigations were performed on 10 members of the family, and these confirmed the diagnosis of haemophilia, the thromboplastin generation test indicating a defect which was corrected by isolated anti-haemophilic globulin. No other anomalies in the clotting mechanism were found in the family. The father of one of the female propositi in Generation VI was normal on testing; the father of the other was not available, but was reported to have no personal or family history of bleeding diathesis.

The authors suggest three possible explanations: (1) a spontaneous mutation on a previously normal X chromosome; (2) that the trait has recently assumed a dominant character in this family; and (3) non-disjunction of the maternal sex chromosomes during meiosis, the resulting zygote in the offspring being XXX and the daughters thus having two affected chromosomes.

R. H. Cawley

707. **The Sex Ratio of Mutation Rates of Sex-linked Recessive Genes in Man with Particular Reference to Duchenne Type Muscular Dystrophy**
E. A. Cheeseman, S. J. Kilpatrick, and A. C. Stevenson. *Annals of Human Genetics* [*Ann. hum. Genet.*] **22**, 235–243, May, 1958. 14 refs.

Public Health and Industrial Medicine

708. **The Mortality from Arteriosclerotic and Hypertensive Heart Diseases in the United States. I. Possible Relation to Distribution of Population and Economic Status**

L. H. SIGLER. *American Journal of Cardiology* [*Amer. J. Cardiol.*] **1**, 176–180, Feb., 1958. 5 refs.

In the United States in 1950 the over-all mortality from arteriosclerotic heart disease was 213·0 per 100,000 population and that from hypertensive heart was 56·5 per 100,000, although the figures for individual States varied widely. In the study herein reported the author examines this variation and attempts to relate it to population distribution and to economic status.

The mortality rate from arteriosclerotic heart disease was everywhere far higher than that from hypertensive heart disease, but there was no parallelism between the two rates in different States. A positive relationship, however, appeared to emerge between the mortality from arteriosclerotic heart disease and the population density in different parts of the country, especially the proportion of people living in towns. There was no similar correlation between these factors and mortality from hypertensive heart disease, and the average income per head of the population was not definitely related to either death rate.

It is suggested that these results point to differences in mode of living, other than dietetic, as factors in the aetiology of arteriosclerotic heart disease. These differences do not seem to have the same influence on the pathogenesis of hypertensive heart disease.

S. G. Owen

709. **Bronchitis Mortality Rates in England and Wales and in Denmark**

O. W. CHRISTENSEN and C. H. WOOD. *British Medical Journal* [*Brit. med. J.*] **1**, 620–622, March 15, 1958. 2 figs., 11 refs.

The recorded mortality from bronchitis in England and Wales is much higher than in other countries of Europe and in the U.S.A., being about 10 times higher than in Denmark. Even when the maximum allowance is made for differences between the British and Danish rules for certification of the cause of death there is still a marked excess of deaths from bronchitis in England and Wales.

In an attempt to account for this difference the authors discuss the operation in the two countries of certain factors which might be considered to influence the incidence of bronchitis, namely—standard of living; urban and rural residence; age and sex distribution; climatic conditions; and tobacco consumption. In respect of the first four of these, conditions are very similar in England and Wales and in Denmark; only in respect of the last factor is there a marked discrepancy. Whereas the annual consumption of tobacco per head since 1905 has been lower in England and Wales than in Denmark, except for the war years, the amount smoked in the form of cigarettes has always been twice as large. It would appear, therefore, that the national smoking habits rather than the amount of tobacco consumed per head of population may contribute to the excessive mortality from bronchitis in England and Wales. *M. Maclean*

710. **Observations on the Medical Condition of Men in the Seventh Decade**

R. G. BROWN, T. MCKEOWN, and A. G. W. WHITFIELD. *British Medical Journal* [*Brit. med. J.*] **1**, 555–562, March 8, 1958. 5 figs., 12 refs.

In this study, reported from the Department of Social Medicine, University of Birmingham, 1,062 out of the 1,243 men aged 60 to 69 years on the lists of 11 Birmingham general practitioners were examined by the latter as if for life insurance and also with reference to their employment and fitness for work. The sample agreed quite closely with the age and social class structure of this decade of the population, as shown by the 1951 Census figures. Only significant diseases were considered, and these were reckoned disabling only if they appreciably interfered with the life of the individual. The aim of the study was to guide policy in regard to retirement by relating physical capacity to age.

Some type of disease was present in 4 out of every 5 men, but in nearly half the total there was no disability. The incidence of both disease and disability rose with age, the incidence of disability sufficient to restrict or prohibit employment rising from 1 in 10 at age 60–61 to 1 in 5 at age 68–69. The commonest diseases were bronchitis, defective hearing, and coronary arterial disease, and the three commonest causes of disability were bronchitis, coronary disease, and osteoarthritis. The incidences of disease and disability were closely related to social class (as determined by occupation), increasing regularly from the Registrar-General's Class I to Class V. The incidence of 6 of the 8 commonest diseases was similarly related to social class, though in regard to bronchitis this trend did not apply to non-smokers. All cases of suspected coronary disease were referred for cardiological examination. The incidence of coronary manifestations other than coronary occlusion increased regularly from Class I to Class V, that is, in the opposite direction to the trend of mortality from this disease.

In assessing fitness for work the authors were concerned only with the ability of individuals at various ages to contribute effectively to production. The difficulties of defining the original work of a man who has often changed occupation are emphasized. Only fitness for full-time work in a man's original work or in a similar type of work was considered. Of those in their 66th year, 3 out of 4 men were still at work. Retirement

before the age of 65 was attributable to ill-health in 64% of cases, but after 65 it accounted for only 33%. Financial need was the main reason for continuing work in 78% of cases, especially in Class V. The proportion of those unfit for employment was 1 in 10 of the whole sample, but in the last year (68–69) one out of every 4 was unfit. Among men over the age of 65 unfitness was closely related to social class, and in the age group 65–69 only 4·4% were fit and willing for employment, after those still working had been excluded. Nevertheless the authors conclude that there are no medical grounds for prohibiting an increase in the retirement age to beyond 65, and that to increase it would only be to rationalize a set of circumstances already existing.

J. N. Agate

711. **The Survival of *Rickettsia burneti* in Water and Methods of Sterilisation.** (К вопросу о выживаемости риккетсий Бернета в воде и методах ее обеззараживания)

S. M. Kulagin, N. I. Fedorova, and N. F. Sokolova. *Журнал Микробиологии, Эпидемиологии и Иммунобиологии* [*Z. Mikrobiol.* (*Mosk.*)] **29**, 62–66, No. 2, Feb., 1958. 12 refs.

Rickettsia (*Coxiella*) *burneti* is known to survive for long periods in milk, blood, and urine. The length of its survival in drinking water, another possible source of infection, was therefore studied at the Gamaleya Institute of Epidemiology and Microbiology of the Academy of Medical Sciences of the U.S.S.R. Autoclaved water from a piped water supply was infected with dried material containing one particular laboratory strain of rickettsiae in two dilutions, 10^{-3} and 10^{-6}. The infected water samples were kept at 18 to 20° C. and at 4° C. and at set intervals 0·5 ml. of each was injected into the yolk sac of 6- or 7-day-old chick embryos, which were then candled daily. Any embryos found dead on candling were opened and smears were made from the yolk sac and stained for rickettsiae. The contents of such yolk sacs in which no rickettsiae were found on microscopical examination and of the yolk sacs of embryos surviving for 14 days were passed three times through fresh chick embryos for enrichment.

In the water sample with the heavier inoculum rickettsiae survived at both temperatures for 160 days, when the investigation was discontinued, while in the sample with the lighter inoculum they survived for 100 days at 18° to 20° C. and for 140 days at 4° C. Thus the survival of rickettsiae in water is of the same order as that of *Brucella* spp., though possibly less than that of intestinal pathogens of the *Salmonella* group, and it is concluded that the possibility exists that Q fever may be contracted from an infected water supply.

Boiling killed the strain of *R. burneti* used within one minute. Chlorine in a concentration of 200 mg. per litre of water is known to kill *R. burneti* within 3 to 5 minutes. In the present experiments the water sample infected more heavily became non-infectious within 30 minutes at a chlorine concentration of 100 mg. per litre, within 2 hours at 50 mg. per litre, and within 10 to 12 hours at 10 mg. per litre. The more lightly infected water sample became non-infectious within 10 minutes at a chlorine concentration of 50 mg. per litre, within 30 minutes at 20 and at 10 mg. per litre, and in 10 to 12 hours at 5 mg. per litre, but remained infectious for 24 hours at a chlorine concentration of 1 mg. per litre.

K. Zinnemann

EPIDEMIOLOGY AND IMMUNIZATION

712. **Large Epidemic Outbreak of Vomiting Associated with Meningism and Exanthem. Clinical and Epidemiological Observations**

I. Ash. *British Medical Journal* [*Brit. med. J.*] **1**, 316–318, Feb. 8, 1958. 25 refs.

In the autumn of 1956 an outbreak of a disease resembling epidemic nausea and vomiting occurred in Harlow, Essex. Precipitate vomiting was often accompanied by anorexia, abdominal pain, headache, and diarrhoea. In some patients meningism developed and examination of the cerebrospinal fluid revealed lymphocytosis and an increase in the protein concentration. In other cases lymphadenopathy or a rubella-like exanthem was observed. Injected fauces were frequently found, suggesting a respiratory portal of entry of the infection. Infectivity was high, since multiple cases in the same household were common. The incubation period was about 2 days. The author states that the causative agent is believed to be a virus, but that it has not yet been isolated. The differential diagnosis of this condition from aseptic meningitis and non-paralytic poliomyelitis is discussed.

D. Geraint James

713. **Trials of an Asian Influenza Vaccine**

Fourth Progress Report to the Medical Research Council by its Committee on Influenza and Other Respiratory Virus Vaccines. *British Medical Journal* [*Brit. med. J.*] **1**, 415–418, Feb. 22, 1958. 3 refs.

The results are reported of serological and field trials of a vaccine of the Asian strain of influenza virus A/Singapore/1/57. This was prepared in four strengths containing 20,000 and about 14,000, 7,000, and 3,500 haemagglutinating units (h.u.) of virus per ml. respectively absorbed on to 10 mg. of aluminium phosphate, the dose being 1 ml. injected subcutaneously. (The American chick cell agglutinating (C.C.A.) unit is equivalent to between 25 and 40 h.u.)

The serological trial was carried out on four groups of about 60 young men, each receiving a single dose of one of the vaccines. A haemagglutination inhibition test was performed 3 weeks after the inoculation, the geometric mean antibody titres in the four groups being 14·9, 7·6, 9·8, and 7·2 respectively. These comparatively low titres were possibly partially due to sensitivity of the virus to non-specific inhibitory factors in the serum. A second dose was given 3 to 4 weeks after the first to 20 subjects in the groups receiving 20,000 and 7,000 h.u., when the geometric mean titres rose to 77·7 and 56·5 respectively.

The aim of the field trial was to compare the values of the following dosages of the Asian vaccine (1) 2 injections

of 7,000 h.u. each, (2) a single injection of 7,000 h.u., and (3) a single injection of 20,000 h.u. As controls a polyvalent vaccine prepared from older A strains and an influenza B vaccine were used. A total of 3,093 persons, drawn from boys' public (boarding) schools, teachers' training colleges, and miscellaneous centres were inoculated. In several centres influenza epidemics started shortly before or shortly after the date of inoculation, and it was therefore not possible to judge the effect of 2 doses as compared with one. The figures from the public schools show that in the first few days after inoculation there was no difference in the incidence of clinical influenza between the groups receiving the three different vaccines, but during the period 9 to 15 days after inoculation the incidence of influenza among boys vaccinated with the Asian type of vaccine was only about one-third of that in the control groups, giving a protection rate of 66%. In the teachers' training colleges the protection rate was 75% and in the miscellaneous centres 50%. The dose of vaccine used in the public schools was 20,000 h.u., and in the training colleges and other centres 7,000 h.u. There was no significant difference in the incidence of Asian influenza between groups given the two control vaccines. *F. Hillman*

714. **Autogenous Vaccine in Prophylaxis of the Common Cold**
J. M. RITCHIE. *Lancet* [*Lancet*] **1**, 615–618, March 22, 1958. 1 fig.

Acting on the theory that many of the more unpleasant symptoms of the common cold are due to infection by commensals acting on a mucous membrane rendered more susceptible by the virus infection the author, working at the Public Health Laboratory, Birkenhead, prepared cultures on blood agar from the saliva and swabs from the nose and throat of some 200 volunteer subjects. The whole of the growth, suspended in carbol saline and inactivated at 60° C. for 30 minutes, was used to constitute the vaccine, which was then administered in gradually increasing doses at weekly intervals to 109 of the subjects. A control group, numbering 75, received the same dosage of carbol saline only.

Assessment of the results showed that the cold rate per month among the controls was five times that among the subjects who received the full course of immunization. Absence from work because of colds was also higher in the control group. The author, who was originally sceptical of the value of such autogenous vaccines, concludes that the results indicate that the vaccine conferred some form of protection, which was lost if the treatment was stopped too soon. *R. Hare*

715. **Antibody Responses to British Poliomyelitis Vaccine of Children with Naturally Occurring Antibody**
K. RUSSELL. *British Medical Journal* [*Brit. med. J.*] **1**, 622–624, March 15, 1958. 1 fig., 3 refs.

Specimens of serum were obtained in London and Manchester from 254 children aged one to 9 years before immunization against poliomyelitis and again 14 days after the second of two injections of British formalinized poliomyelitis vaccine given 4 weeks apart. Antibody titrations were carried out against each of the same strains of virus as were used for the vaccine—Brunenders for Type 1, MEF–1 for Type 2, and Saukett for Type 3—lack of inhibition at a dilution of 1:8 being regarded as a negative result.

Before vaccination 66 of the 254 sera gave completely negative results; of the remainder, 55 contained antibodies against one type, 67 against 2, and 64 against all 3 types. The results obtained after vaccination showed that where there was pre-existing homologous antibody the average response was much higher, whereas the effect of pre-existing heterologous antibodies varied. Thus enhancement of the response to Type 3 occurred only when both heterologous antibodies were present, the response to Type 1 was increased in the presence of Type-2 but not of Type-3 antibody, while the response to Type 2 was increased when antibody against either Type 1 or Type 3 was present.

[Unfortunately an epidemic of Type-1 poliomyelitis was occurring in Manchester at the time the sera were taken, but separate results for the two cities are not given.] *W. K. Dunscombe*

716. **Efficacy of Poliomyelitis Vaccine, with Special Reference to Its Use in Minnesota in 1955–1956**
L. M. SCHUMAN, H. KLEINMAN, L. J. KROVETZ, and D. S. FLEMING. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **166**, 1027–1035, March 1, 1958. 2 figs., 14 refs.

An attempt was made to assess the efficacy of poliomyelitis vaccine on the basis of information collected in Minnesota, where administration of the Salk vaccine was begun in May, 1955, first to children in the age group 6 to 9 years and then extended in 1956 to all children and adolescents under 19 years of age. By the end of 1956 66·2% of the population under 19 years had received at least one dose of vaccine. The authors point out that because of changes in methods of vaccine production since the mass field trial in 1954, the efficacy of the Salk vaccine has been continuously studied in Minnesota.

Using the usual methods of comparison the authors found that the results were difficult to interpret. Although the incidence of proven cases of poliomyelitis fell from 131·6 per 100,000 population in 1952 to 4·5 per 100,000 in 1956, the latter rate was not significantly different from that of 6·7 per 100,000 for 1947, and might merely be due to the tendency to fluctuation in annual incidence of the disease. The incidence of paralytic poliomyelitis in 1956 was, however, only 2·1 per 100,000, which was half the lowest incidence recorded in the preceding 10 years. Further, the ratio of paralytic to non-paralytic cases in 1955–56 was only slightly lower than the fairly stable ratio in the preceding 8 years. A study of the age distribution of cases showed that the curve of the incidence of paralytic disease, which had shown a peak in the age group 5 to 9 years, had flattened out. (In New York State the peak incidence of paralytic poliomyelitis had shifted to the age group 0 to 5 years.) When a " life-table " method was used in analysing the incidence of poliomyelitis in vaccinated and non-vaccin-

ated groups it was apparent that with two doses of vaccine there was a significant reduction in the incidence of the paralytic form of the disease, from 7·7 per 100,000 among the non-vaccinated to 1·3 among the vaccinated receiving two doses. With a single dose of vaccine no significant reduction was observed. *A. Ackroyd*

717. **Influence of Prior Active Immunization on the Presence of Poliomyelitis Virus in the Pharynx and Stools of Family Contacts of Patients with Paralytic Poliomyelitis**

P. F. WEHRLE, R. REICHERT, O. CARBONARO, and B. PORTNOY. *Pediatrics* [*Pediatrics*] **21**, 353–361, March, 1958. 2 refs.

At the State University of New York College of Medicine, Syracuse, examination of the stools of 50 of the 55 family contacts of 12 patients with paralytic poliomyelitis who had demonstrable poliovirus in the faeces or pharyngeal secretions or both revealed that poliovirus was present in 8 (57%) of the 14 immunized contacts and in 21 (58%) of the 36 non-immunized contacts. Isolation of virus was accomplished less frequently in the age group 5 to 9 years than among the other childhood age groups, this being the age group to which the Salk vaccine was initially given. There was no striking difference in the distribution of titres of virus in the faeces of the index patients and the immunized and non-immunized contacts.

Only 3 samples from 2 different contacts yielded barely detectable quantities of virus among 52 samples of pharyngeal secretions obtained from immunized contacts at 3-day intervals for 9 days after the admission to hospital of the index patient, whereas 15 of the 88 samples from the non-immunized child contacts yielded poliovirus, several in high titre. The isolation of virus from the pharyngeal secretions of the non-immunized contacts was accomplished with equal frequency throughout the course of the study, but in the case of the immunized contacts only initial samples yielded virus. Previous tonsillectomy did not appear to have any influence on the likelihood or otherwise of recovering poliovirus from the pharynx. The authors conclude that the apparent diminution in both the incidence and concentration of poliovirus in the pharynx of persons with poliomyelitis infection acquired after immunization may be important in the epidemiology of this disease among an immunized population in which high standards of environmental sanitation are observed and good personal hygiene is practised. *A. Ackroyd*

718. **Report on Examination of Home Contacts of Poliomyelitis**

REPORT OF THE PUBLIC HEALTH LABORATORY SERVICE. *Monthly Bulletin of the Ministry of Health and the Public Health Laboratory Service* [*Monthly Bull. Minist. Hlth Lab. Serv.*] **17**, 58–64, March, 1958. 3 refs.

During the summer and autumn of 1956 attempts were made to isolate poliovirus from the faeces of 96 cases of poliomyelitis and 290 household contacts. Poliovirus was isolated from 77% of 74 paralytic patients from whom faeces were obtained, and from 27% of contacts of all cases. The proportion of excreters among the contacts was inversely in relation to age. Under 5 years of age the proportion was 63%, between 5 and 15 years 36%, and over 15 years 9%. The proportion was higher in contacts of cases which were shown to be excreting virus than in those which were not—30% as against 18%. The length of time elapsing between the onset of illness in the primary case and the examination of faeces from the contact made little difference to the chances of finding the virus; the proportion was just as high in specimens examined 3–4 weeks after the onset as during the first week.

Taken in conjunction with epidemiological findings these results tend to support the view that both the primary case and the contacts are usually infected at about the same time from the same source. By the time the primary case is diagnosed, infection has already been disseminated throughout the household, and the taking of prophylactic measures, such as the injection of gamma globulin is superfluous.—[Authors' summary.]

719. **Toxin Food-poisoning Caused by Fried Potatoes**

J. B. M. DAVIES and W. H. PARRY. *Lancet* [*Lancet*] **1**, 684–686, March 29, 1958. 1 ref.

The authors report 8 cases of acute diarrhoea and abdominal pain, accompanied in 2 of them by vomiting, following consumption of a meal in a restaurant in Liverpool. The foodstuffs common to all 8 meals were fried chipped potatoes and tinned peas. A diagnosis of staphylococcal toxin food poisoning was based on the recovery of *Staphylococcus aureus* from vomit and faeces in 2 cases admitted to hospital, the incubation period in these cases being 30 minutes to 4½ hours. Bacteriological examination of tins of peas from the same batch as that used in the restaurant proved negative. Of the 15 members of the restaurant staff, 11 were found to be carriers of staphylococci, and 4 of these, including the cook, had uncovered septic skin lesions. The chipped potatoes were prepared by hand, partly cooked in groundnut oil at 350° F. (176·6° C.) for 1 to 3 minutes, and then left exposed in the kitchen until required, which sometimes was as long as 24 hours; they were subsequently cooked for a further 5 to 8 minutes.

Experiments were carried out to determine the degree of staphylococcal survival on cooked chipped potatoes " under café conditions ". It was found that although frying at 320° F. (160° C.) for 2 minutes killed an inoculum (0·1 ml. of a suspension of *Staph. aureus*), re-inoculation of the partly cooked chips resulted in growth in all specimens. It was estimated that within 24 hours the staphylococci had increased 1,000-fold, indicating that the potato is a good culture medium. When re-inoculated chips were cooked a second time at intervals up to 24 hours, sporing organisms were found in two specimens examined after 1 and 12 hours respectively.

The outbreak was attributed to contamination of partly cooked chips, the final cooking of which did not destroy the heat-stable enterotoxin. The authors draw attention to the faults which led to this small outbreak—poor hygiene, storage of partly cooked food while warm, and ignorance of the heat-resisting property of staphylococcal enterotoxin. *V. Reade*

720. **Food Poisoning in the Russian Socialist Federal Soviet Republic.** (Пищевые отравления в РСФСР за 1956 г.)
E. S. KRASNICKAJA. *Гигиена и Санитария* [*Gig. i Sanit.*] **23**, 49–53, No. 3, March, 1958.

Though the number of outbreaks of food poisoning in the R.S.F.S.R. in 1956 was lower than in previous years, the total number of patients involved was rather higher and children accounted for 30·2% of them, a slight increase on previous years. The highest incidence occurred in June and July, 30% of all the cases occurring in these 2 months. The number of outbreaks in places with communal feeding diminished somewhat but still remained high, especially in children's institutions.

The aetiology of the food poisoning was considered to be bacterial in 69·4% of cases, non-bacterial in 12·5%, and was undetermined in 18·1%. The foods chiefly responsible were meat products, which accounted for 40·2% of cases of bacterial aetiology, followed by milk and milk products (26·5%). Bacteriologically, the following micro-organisms were incriminated: *Clostridium botulinum*, salmonellae, staphylococci, streptococci, and *Shigella sonnei* and *newcastle* causing dysentery. The number of infections due to salmonellae was less than in previous years, but these organisms still accounted for 13% of the total number of bacterial cases confirmed in the laboratory. Two-thirds of these infections were attributed to meat products, a few to milk and yoghourt, and one to duck eggs. The number of cases of staphylococcal food poisoning has increased year after year, these organisms being found in 25% of all cases examined. The year 1956 was a good one for mushrooms, and consumption of the non-edible varieties of fungi caused a considerable number of cases of toxicosis, with a relatively high mortality. Cases of food poisoning were also reported to have occurred from the use of grain or flour contaminated with mouse poisons; these cases were generally severe and had a mortality of 7·6%. The author urges tightening up the veterinary control of the slaughter of cattle for meat as one method of reducing the incidence of food poisoning, especially the number of outbreaks due to salmonellae. *Basil Haigh*

721. **The Casper Project—an Enforced Mass-culture Streptococcic Control Program. I. Clinical Aspects**
B. PHIBBS, D. BECKER, C. R. LOWE, R. HOLMES, R. FOWLER, O. K. SCOTT, K. ROBERTS, W. WATSON, and R. MALOTT. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **166**, 1113–1119, March 8, 1958. 4 figs., 7 refs.

Since 1954 a campaign to reduce the incidence of haemolytic streptococcal infection and of acute rheumatism and acute nephritis has been in operation in the town of Casper, Wyoming, among the 6,460 children attending primary schools. All such children with any symptoms of an upper respiratory infection are inspected daily and swabs from the nasopharynx are cultured, those children from whom haemolytic streptococci are isolated being excluded from school until antibiotic therapy has been instituted or negative swabs obtained in the case of refusal of such treatment. One intramuscular injection of 600,000 units of benzathine penicillin, 3 injections of 300,000 units of penicillin in aluminium monostearate, or 10 days of oral penicillin therapy is regarded as adequate.

These procedures have resulted in a marked fall in the incidence of streptococcal infection. When the programme is interrupted, as by school holidays, there is a marked rise in the infection rate, which falls again as control is re-established. The effect on the occurrence of acute rheumatism and acute nephritis is difficult to assess, but no cases of acute nephritis have occurred and only 5 of acute rheumatism in the population concerned since the start of the campaign. The latter figure is about one-tenth of what might have been expected. Moreover, of the 5 cases of acute rheumatism, one occurred in a child who was away from home at the time and one in a child who concealed the fact that he had a sore throat and whose throat was therefore not swabbed. *C. Bruce Perry*

722. **The Casper Project—an Enforced Mass-culture Streptococcic Control Program. II. Technical Aspects**
D. BECKER, B. PHIBBS, and C. LOWE. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **166**, 1119–1123, March 8, 1958. 7 refs.

A description is given of the bacteriological techniques adopted and administrative details necessary to enable the scheme to control haemolytic streptococcal infection in the schools of Casper, Wyoming, [see Abstract 721] to be put into effect. By simplifying laboratory procedures it was possible to reduce the cost considerably, while the investigation of children with symptoms of upper respiratory infection and the taking of swabs was carried out largely by voluntary workers and was so arranged that it did not materially interfere with school routine.

[For practical details the original paper should be consulted.] *C. Bruce Perry*

723. **Serum Prophylaxis of Botkin's Disease [Infective Hepatitis] in Institutions for Children in Rostov-on-Don.** (Серопрофилактика болезни Боткина в детских учреждениях города Ростова-на-Дону)
T. I. FADEEVA. *Журнал Микробиологии, Эпидемиологии и Иммунобиологии* [*Z. Mikrobiol. (Mosk.)*] **29**, 21–23, No. 4, April, 1958.

The prophylactic injection of γ globulin (0·2 ml. per kg. body weight) brought about a reduction in the incidence of infective hepatitis among groups of contacts in children's crêches in Rostov-on-Don, the incidence of secondary cases of the disease being 6½ times higher in control groups well matched for age, size, and degree of exposure. In a few children to whom the prophylactic injection could be administered within 3 days of the occurrence of the first case the incidence was 8 times less than in the control groups, whereas the administration of γ globulin more than 10 days after the first clinical manifestation of infective hepatitis in a closed community of children had little effect. The same principles

apply to measles antiserum, which can be used in the prophylaxis of infective hepatitis. The passive immunity conferred lasts for 6 to 8 weeks, so that if secondary cases occur the injections must be repeated after this period. *K. Zinnemann*

INDUSTRIAL MEDICINE

724. **Lung Function in Silicosis of the Witwatersrand Gold Miner**

M. R. Becklake, L. du Preez, and W. Lutz. *American Review of Tuberculosis and Pulmonary Diseases* [*Amer. Rev. Tuberc.*] **77**, 400–412, March, 1958. 2 figs., 25 refs.

The chest radiographs of all men between the ages of 41 and 60 attending the Pneumoconiosis Bureau of the South African Council for Scientific and Industrial Research, Johannesburg, between December, 1955, and May, 1956, were examined and two groups of cases selected for study—those with a normal radiological pattern and those with radiological evidence of generalized silicosis with small or medium nodulation. Miners with less than 7 years' service underground, with more than 6 months' service in mines outside the Witwatersrand area, or with inadequate records were rejected. From the remainder a random sample was taken of 10 subjects aged 41 to 50 and 10 aged 51 to 60 in each radiological group. These 40 miners were all subjected to an elaborate battery of lung function tests giving a total of 20 measurements for each man, details of which are given in tables.

Statistical analysis confirmed the impossibility of discriminating significantly between those with and those without radiological abnormality by means of any single physiological test, but a discriminant analysis applied to the results of 8 selected tests showed that the two groups could be separated with only 13% overlap. No smaller number of tests could be regarded as giving a satisfactory screening procedure for distinguishing disability due to silicosis. There was a significant association between the number of years of work on rock-breaking and the lung function score. The clinical estimate of degree of dyspnoea did not correlate significantly with the lung function score, but did so with the Hugh-Jones dyspnoeic index.

The detailed results are compared with those of previously published investigations, but the validity of this comparison is limited by the great distortion introduced by differences in the criteria for selection of cases. Since the criteria for selection in the present series were somewhat similar to those used by Gilson and Hugh-Jones in their study of pulmonary function in South Wales coal-miners (*Spec. Rep. Ser. med. Res. Coun. (Lond.)*, 1955, No. 290), however, values for vital capacity and maximum breathing capacity in the two groups are compared. It is concluded that there is a slightly greater deterioration in both these functions with the development of nodular silicosis, as in the Rand gold-miner, than with the development of coal-workers' pneumoconiosis of equivalent radiological grade. [Since it has been shown in more recent work by the M.R.C. Pneumoconiosis Research Unit that the change of maximum breathing capacity with radiological category is profoundly affected by the type of population studied, even among coal-workers, the implication that this difference is attributable to differences in aetiology does not seem to be justified.] The correlation between lung function score and rock-breaking service is regarded as suggesting that respiratory disability due to mining could be demonstrated in men without radiological evidence of dust disease. [This conclusion would also seem to be unjustified, since data from men with radiological evidence of disease were used in calculating the correlation between rock-breaking service and the lung function index.] *C. M. Fletcher*

725. **Parathion Residues as a Cause of Poisoning in Crop Workers**

G. E. Quinby and A. B. Lemmon. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **166**, 740–746, Feb. 15, 1958. 16 refs.

The authors give a well documented account of 12 episodes of parathion poisoning involving over 70 workers engaged in the fruit-growing industry in the States of California and Washington, where parathion is used as a pesticidal spray. Those affected were not engaged in the actual spraying, but worked among the crops after the spraying. The parathion appears to have been absorbed by the dermal route, owing to the persistence of toxic residues on the trees and vines. The nature of the illness was confirmed in most cases by the changes in blood cholinesterase level and the therapeutic response to atropine. The longest interval between spraying and poisoning in a proved case was 33 days. The route of entry, the environmental factors predisposing to poisoning, and the preventive measures which should be taken are discussed. *H. B. Stoner*

726 (a). **Occupational Hygiene of Female Benzene Workers.** (Гигиена труда и состояние здоровья женщин, работающих с бензолом)

V. A. Kajanovič, Z. I. Koževnikova, I. L. Miropolskaja, N. P. Mihajlova, A. I. Fadeeva, and D. N. Fomičeva. *Гигиена Труда и Профессиональные Заболевания* [*Gig. Truda prof. Zabolev.*] **2**, 26–31, No. 1, Jan.–Feb., 1958. 14 refs.

726 (b). **The Effects of Benzene on Lactating Female Experimental Animals and Their Offspring.** (Данные о влиянии бензола на лактацию самок и организм новорождённых экспериментальных животных)

D. I. Horošanskaja. *Гигиена Труда и Профессиональные Заболевания* [*Gig. Truda prof. Zabolev.*] **2**, 31–35, No. 1, Jan.–Feb., 1958. 4 figs., 8 refs.

The first of these two papers from the Gorky Institute of Occupational Hygiene and Diseases describes an investigation into the health of 100 pregnant or lactating women employed at a plant producing benzene. The usual concentration of benzene in the working environment was 0·05 to 0·1 mg. per litre. In a number of cases typical blood changes of moderate benzene poisoning were present, but the investigation was directed mainly

to the state of the female reproductive system, which is rarely mentioned in the literature on benzene poisoning. Comparison with a control group of non-pregnant women working in the same conditions revealed no evidence of specific lesions affecting the reproductive organs or of any changes in the ovarian and menstrual cycles or in the normal course of pregnancy. It was noted, however, that when lactating women were working with benzene the infants of 41·6% of them had to be fed artificially (compared with 6·4% in the control group) because of their refusal to take the breast. It is suggested that this could probably be accounted for by the fact that the milk contained from 0·63 to 9·68 μg. of benzene per 100 ml.

In a study of the influence of benzene on lactation reported in the second paper experiments were carried out on pregnant and lactating white rats and guinea-pigs, these animals being exposed to a benzene concentration of 0·05 to 0·1 mg. per litre, that is, the concentration present in the industrial plant. These studies showed that the vitamin-C content of the milk of the guinea-pigs was lowered, although the vitamin-C content of the organs of the offspring was not changed. In the rats the content of free vitamin C in the maternal milk was reduced, but the combined vitamin-C content was increased, while in the organs of the suckling rats the levels of both forms of vitamin C were raised, probably as a result of increased synthesis of the vitamin. Lactation was depressed and the growth of the young animals was retarded. The author concludes that while there is no particular hazard in the employment of pregnant women on processes involving exposure to benzene, this type of work is not suitable for women who are breast-feeding their infants. *Basil Haigh*

727. **Haematopoiesis in the Bone Marrow in Chronic Benzene Poisoning.** (К вопросу о костномозговом кровотворении при хронической интоксикации бензолом)

I. M. Omel'janenko. *Гигиена Труда и Профессиональные Заболевания* [*Gig. Truda prof. Zabolev.*] **2**, 35–40, No. 1, Jan.–Feb., 1958. 11 refs.

Between 1946 and 1955 a total of 90 patients (70 males and 20 females) were treated at the clinic of the Institute of Occupational Hygiene and Diseases, Moscow, for benzene poisoning. Their ages varied from 18 to 50 years and the period of exposure to benzene from 1½ months to 24 years.

The state of haematopoiesis in the bone marrow of the patients, as ascertained by puncture biopsy examination, is summarized as follows. Although the findings were variable, in most cases there was a fall in the number of myelokaryocytes and some degree of hypoplasia, the severest cases showing aplasia of the marrow, while in a few cases there was a slight increase in the number of myelokaryocytes. In both types of case there was retardation of maturation of all 3 haematopoietic processes in the bone marrow. Many cells showed signs of degeneration and there was an increase in the number of plasma cells and reticulo-endothelial cells, and sometimes also of lymphocytes and monocytes. It was observed that when the number of reticulocytes fell in the peripheral blood their numbers in the bone marrow might be increased, sometimes considerably. The number of megakaryocytes in the bone marrow was notably diminished and in the severest cases they could not usually be found in marrow smears.

It is stressed that the study of the bone marrow is a vital part of the examination of patients with chronic benzene poisoning, and is especially valuable in assessing the response to treatment and in determining the prognosis. It is pointed out that the peripheral blood picture does not always reflect the true state of the bone marrow in these patients. *Basil Haigh*

728. **The Clinical Features of Chronic Benzene Poisoning.** (К вопросу о клинике хронических интоксикаций бензолом)

G. E. Rozencvit. *Гигиена Труда и Профессиональные Заболевания* [*Gig. Truda prof. Zabolev.*] **2**, 41–45, No. 1, Jan.–Feb., 1958. 8 refs.

The author reports his findings in 150 cases of chronic benzene poisoning observed during the period 1952–6. The earliest clinical features in such cases are referable to the central nervous system, and take the form of functional neuroses and asthenia. By the use of special tests, such as the thermoregulatory reflex of Shcherbak, determination of the sensitivity of the skin to ultraviolet light, and thermotopography [details of which are unfortunately not given] abnormalities may be detected at this stage, this lending objective support to the otherwise mostly subjective symptomatology. These abnormal findings, which are described in detail, are especially marked in the case of the thermoregulation test. The author describes this stage of chronic benzene poisoning as one of a "neurasthenic syndrome with autonomic dysfunction". The combination of these findings with the pathological changes in the blood results in a picture which is characteristic of chronic benzene poisoning. A little later the peripheral nervous system is often involved, with the development of polyneuritis, mainly of an autonomic, sensory type, and mainly affecting workers whose hands are constantly contaminated with benzene.

The functional nervous changes of the early stage gradually become converted into organic changes typical of a toxic encephalopathy, being manifested by the appearance of inequality of the pupils, asymmetry of the facial innervation, slight hypomimia, increase in and asymmetry of the tendon reflexes, and absence of the abdominal and plantar reflexes, together with the original asthenic syndrome. In many cases there may also be organic hyperkinesia, which is not due to a localized lesion in the brain but to a diffuse lesion of a subcortical nature. Attention is drawn to the observation that such toxic encephalopathy may not appear until one to 2 years after cessation of contact with benzene. Finally, the fact that these neurological changes precede the blood changes in chronic benzene poisoning points to the importance of a thorough neurological examination as part of the routine periodic medical examination of workers in contact with benzene. *Basil Haigh*

Forensic Medicine and Toxicology

729. **A Percentage Method for Representing the Fall in Body Temperature after Death. Its Use in Estimating the Time of Death. With a Statement of the Theoretical Basis of the Percentage Method.**
F. S. FIDDES and T. D. PATTEN. *Journal of Forensic Medicine* [*J. forensic Med.*] **5**, 2–15, Jan.–March, 1958. 5 figs., 2 refs.

There is no theoretical reason why a dead body, in cooling, should not behave like other solids of similar shape. The authors, working at the University of Edinburgh, have attempted to elucidate the laws which govern the cooling of dead bodies, by means of experiments carried out over more than 4 years on over 100 bodies and by comparing the results with theoretically deduced expressions for a solid cylinder of homogeneous material. Their object was to find a method for the accurate determination of time of death from temperature recordings which would be practical, of more general application than any hitherto used, and theoretically satisfactory.

Among the more important observations which they made in these experiments were that bodies varied considerably in their rate of cooling and that cooling took, on the average, much longer than is commonly stated. As the environmental temperature was approached the rate of cooling became very slow indeed and was erratic in the sense that minor changes in environmental temperature might result in relatively large changes in the rate of cooling. The authors therefore concluded that the last 15% of the difference between normal body temperature and environmental temperature should be disregarded and that the body could be regarded as virtually cooled when its temperature had fallen through the first 85% of that difference. From this emerged the concepts of "virtual temperature difference at the time of death"—that is, 85% of the total difference between rectal and atmospheric temperatures—and "virtual cooling time"—that is the time required for the rectal temperature to fall through the virtual temperature difference.

It was then found that for all bodies there is a constant relation between the fall in temperature expressed as percentage of the virtual temperature difference and time expressed as percentage of virtual cooling time. This relation can be expressed on logarithmic graph paper as a line which is straight except for a slight flattening in its first part, the significance of which has still to be elucidated. It is independent of sex, size, and environment, provided this last remains constant, and it follows closely the theoretically derived curve, similarly expressed, applicable to the rate of cooling at the centre of a solid cylinder. The authors claim that by means of their graph, provided the body has remained undisturbed and there have been no violent fluctuations in atmospheric temperature, the time elapsed since death can be estimated merely by recording the rectal or (preferably) the liver temperature on two or more occasions over several hours and observing the environmental temperature. Further work is in progress on the effect produced by variation in the environment and other factors.

[This is an important contribution to the subject of the estimation of time of death from observations of body temperature.] *Gilbert Forbes*

730. **Electroencephalographic Findings in Acute Carbon Monoxide Poisoning**
M. A. LENNOX and P. B. PETERSEN. *Electroencephalography and Clinical Neurophysiology* [*Electroenceph. clin. Neurophysiol.*] **10**, 63–68, Feb., 1958. 4 figs., 6 refs.

At the Institute of Neurophysiology, University of Copenhagen, the authors have studied the electroencephalographic (EEG) findings in 33 patients (17 men and 16 women) suffering from acute carbon monoxide poisoning due to exposure to coal gas. About half the patients (18) were under 50 years of age and 15 were over 50. The EEG tracing was abnormal in 18 cases, in 10 of which there was diffuse generalized delta activity, in 3 marked (though less severe) generalized slow activity, in one slight slowing, and in the remaining 4 cases there was a slight but nevertheless significant excess of theta activity, particularly in the temporal regions. Some asymmetry of the abnormal discharges was observed in 14 patients.

The degree of EEG abnormality could be closely correlated with the patient's age and with the depth and duration of unconsciousness. Thus 80% of patients over 50 years of age showed abnormal records, while this was true of only 33% of those under 50. The EEG was abnormal in 95% of those who were still unconscious after 7 hours in hospital, but in only 7% of those who recovered consciousness within 6 hours. It was also abnormal in all patients who were comatose or semi-comatose on admission, but only in 25% of those whose consciousness was relatively unimpaired. Full recovery occurred in 12 of the 20 patients with normal or only slightly abnormal records, whereas 5 of the 13 patients with a markedly abnormal EEG died and only 2 in this group recovered completely. However, permanent sequelae were observed in 8 of the patients with normal records and in 6 with abnormal records. Nevertheless it is concluded that the EEG appears to give information of some prognostic value in cases of carbon monoxide poisoning. *John N. Walton*

731. **The Pharmacology and Toxicology of Boron Compounds.** [Review Article]
H. KINGMA. *Canadian Medical Association Journal* [*Canad. med. Ass. J.*] **78**, 620–622, April 15, 1958. 19 refs.

Anaesthetics

732. **Comparative Studies of Tranquilizers Used in Anesthesia**
E. Lear, I. M. Pallin, A. E. Chiron, L. Rousseau, and C. Aochi. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **166**, 1438–1444, March 22, 1958. 5 figs., 13 refs.

The greater part of this paper is devoted to a historical review of the development of pre-anaesthetic medication and a discussion of the action of the drugs used, ranging from Claude Bernard's observations on the effect of morphine to the effects of the most recently synthesized phenothiazine derivatives. The mode of action of the older drugs is compared with that of modern "tranquillizers", and reference is made to reports in the literature that the probable sites of action of the latter are the ascending reticular activating system and the hypothalamus.

The authors then report their findings in some 1,100 patients at the Jewish Hospital, Brooklyn, and Queen's General Hospital, Jamaica, N.Y., who received premedication with chlorpromazine, promethazine, "pacatal" (pecazine), or diphenhydramine, comparing these with the results in a group of 262 patients given morphine with a belladonna derivative, with and without added barbiturate. In their view the newer agents, chlorpromazine in particular, in comparison with narcotics and barbiturates, enable anaesthesia to be maintained in lighter planes without the risks of reflex stress activity, cause less postoperative vomiting, and promote a more gradual and placid re-awakening of the patient. It is pointed out that all these newer drugs produce some hypotension, which may persist into the postoperative period, but they do not mask the signs of postoperative haemorrhage. *Donald V. Bateman*

733. **Levallorphan and Meperidine in Anesthesia. Study of Effects in Supplementation of Nitrous Oxide–Oxygen–Thiopental Sodium Anesthesia**
F. F. Foldes and K. H. Ergin. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **166**, 1453–1458, March 22, 1958. 7 refs.

In a previous paper (*J. Amer. med. Ass.*, 1956, **160**, 168; *Abstr. Wld Med.*, 1956, **20**, 162) the authors described their experience with alphaprodine as a supplement to nitrous oxide anaesthesia, levallorphan being given to antagonize the respiratory effects of the former drug. In the present paper from the Mercy Hospital and University School of Medicine, Pittsburgh, they report a similar study in which meperidine (pethidine) was used to supplement anaesthesia.

A total of 963 unselected patients undergoing various operations were divided into two groups, one group of 462 receiving pethidine only to supplement the nitrous oxide and another group of 501 receiving, in addition, levallorphan in a dose of 0·02 mg. per kg. body weight—that is, in a ratio of 1:100 to the dosage of pethidine. In the second group thiopentone was added if, after about 5 minutes' administration of nitrous oxide–oxygen, a pharyngeal airway was not tolerated. The patients receiving pethidine alone were given thiopentone from the start in doses ranging from 200 to 600 mg. In those cases in which relaxation was required either for intubation or for surgery succinylcholine was administered either in a single dose or by continuous infusion. Supplementary doses of the analgesic (with or without the antagonist) were given as required, with, occasionally, additional thiopentone; respiration was assisted or controlled as necessary.

The results are analysed in terms of "the mg. per minute requirements" of pethidine and thiopentone, the state of consciousness of the patient within a fixed period after the end of the operation, the incidence of postoperative complications, and the analgesics required during the first 24 hours after operation. It is concluded that levallorphan significantly reduces the incidence of pethidine-induced respiratory depression, thus permitting larger doses of the latter drug to be used with correspondingly less thiopentone. There was little difference between the two groups as regards rate of recovery at the end of the operation; the authors add, however, that recovery was more prompt when alphaprodine was given in place of pethidine.
Donald V. Bateman

734. **Endobronchial Anaesthesia with the Carlens Catheter**
A. V. Jenkins and G. Clarke. *British Journal of Anaesthesia* [*Brit. J. Anaesth.*] **30**, 13–18, Jan., 1958. 24 refs.

The authors discuss the advantages of using Carlens's double-lumen catheter for anaesthesia for one lung; over a period of 20 months at the Royal Infirmary, Manchester, Carlens's catheter was used in 330 cases in which some type of lung operation was performed. They state that with this catheter aspiration of secretions is possible and cross-infection and inflation and deflation of the lung undergoing surgery are prevented. Moreover the lateral position can be adopted with safety. The technique is described and the difficulties are clearly stated. [This paper should be read by all concerned with anaesthesia for surgery of the lung.] *Ronald Woolmer*

735. **Diagnostic and Therapeutic Blocks. A Reappraisal Based on 15 Years' Experience**
J. J. Bonica. *Anesthesia and Analgesia; Current Researches* [*Anesth. Analg. curr. Res.*] 37, 58–68, March–April, 1958. 1 fig., 47 refs.

736. **Anesthesia for Great Vessel Surgery**
J. M. Hansen. *Anesthesia and Analgesia; Current Researches* [*Anesth. Analg. curr. Res.*] 37, 69–74, March–April, 1958.

Radiology

RADIODIAGNOSIS

737. **The Myelographic Examination of the Foramen Magnum**

L. I. MALIS. *Radiology* [*Radiology*] **70**, 196–221, Feb., 1958. 26 figs., 10 refs.

The clinical diagnosis of benign tumours in the region of the foramen magnum is often extremely difficult. Even if such a lesion is suspected a satisfactory diagnosis may not be possible without radiological evidence. In this paper techniques for the myelographic examination of such cases are described in considerable detail [which cannot easily be abstracted], with excellent illustrations and diagrams.

The opaque medium used is " pantopaque " (" myodil ") in quantities of 12 ml. or more. With this amount and using the techniques described globulation of the medium has not caused appreciable difficulty. Extension of the head and neck must be carried out with great care, as it is not tolerated well by patients with cervical lesions. Patients giving a positive response to Queckenstedt's test in hyperextension should not be maintained in hyperextension during the examination; extension of the neck should be the minimum necessary for manipulation of the column of medium owing to the danger of producing compression of the cord. *J. MacD. Holmes*

738. **Roentgen Studies of Ventilatory Dysfunction: an Analysis of Diaphragmatic Movement in Obstructive Emphysema**

S. GOLDENTHAL, B. W. ARMSTRONG, and R. M. LOWMAN. *American Journal of Roentgenology, Radium Therapy, and Nuclear Medicine* [*Amer. J. Roentgenol.*] **79**, 279–292, Feb., 1958. 15 figs., 14 refs.

A useful measure of the efficiency of pulmonary ventilation is provided by observation of the amplitude and speed of movement of the diaphragm during the performance of a forced rapid expiration. This procedure is preferable to the evaluation of pulmonary function during the process of quiet respiration, since the basic defect in such a condition as obstructive emphysema is inability to exhale rapidly a large volume of air. Although fluoroscopy will provide this information quite readily, the interpretation of the results is highly subjective and, further, no permanent record is obtained. The authors, working at Johns Hopkins Hospital, Baltimore, have therefore sought for a more objective method of recording the data, using for this purpose a modification of the conventional kymograph. This consists in a specially constructed grid having lead strips 30 mm. in width and spaced 1 mm. apart, movement of the grid being in a transverse direction over a 30-mm.-wide film so as to permit recording of events over a time interval of 4 seconds. Thus the upward movement of the diaphragm is represented as a series of vertical bands in such a way that a sloping opacity is recorded, the steepness of the slope being a measure of the speed of ascent of the diaphragm and the amplitude of the diaphragmatic movement being obtained by noting the level at which the curve of the slope becomes horizontal. Each record usually contains at least three single wave crests for each leaf of the diaphragm, three of these bands thus providing data for three points on the diaphragmatic surface.

Examination of 20 normal subjects by this method showed a maximum diaphragm excursion ranging from 4·8 to 8·6 cm., with an average value of 6·6 cm. for the right diaphragm and 7·7 for the left. The slope of the curves obtained in these normal subjects was at first very steep, the average normal rate indicating a diaphragmatic rise of 89% of the maximum excursion within the first second. The method was then employed in testing 47 patients suffering from ventilatory dysfunction. (Kymograms of 7 of these cases are reproduced with explanatory diagrams.) Various abnormalities of the curve, such as reduction in amplitude and loss of steepness as well as certain characteristic irregularities, are described. Predictions of percentage ventilation of each lung by this method have shown, the authors state, excellent correlation with the results of pulmonary function tests; this subject will be discussed in a further communication. *A. M. Rackow*

739. **Bronchiolar-cell Carcinoma**

J. H. WOODRUFF, R. E. OTTOMAN, and F. ISAAC. *Radiology* [*Radiology*] **70**, 335–348, March, 1958. 7 figs., 30 refs.

The clinical, pathological, and radiological features of bronchiolar-cell carcinoma (alveolar-cell carcinoma) are discussed, together with the findings in 16 cases. This primary lung tumour of unknown aetiology may present as a solitary focus in the lung or may be multiple when first detected. It may metastasize into the lung on the same or opposite side, and metastases have been reported in the mediastinal lymph nodes, liver, abdominal lymph nodes, bones, adrenal glands, brain, pleura, kidneys, and spleen. Microscopically, the tumour appears as a number of alveolar elements lined with tall columnar or cuboidal cells.

The age incidence is from 16 to 89, 85% of patients being between 30 and 70. Progressive cough is the most common symptom and may be non-productive or may produce copious mucoid sputum. Secondary infection may occur, and there is occasionally haemoptysis. Dyspnoea, chest pain, and weight loss are other common signs or symptoms.

The radiological features are very variable. Single growths tend to develop in a concentric manner and expand the lung rather than infiltrate it; massive atelectasis is not common. When the lesions are multiple the shadows take the form of a nodular infiltration with,

possibly, areas of lobular or segmental collapse. Pleural effusions are common and may obscure the primary lung tumour. Cavitation may be present, but is not usual.

Firm diagnosis may not be possible without surgical exploration, but the authors stress the importance of keeping this condition in mind in the presence of a chronically developing nodular infiltration of the lungs. They also stress the fact that small lesions which may resemble scars and remain unchanged for periods of more than a year may show evidence of growth and dissemination in due course, and reveal themselves as bronchiolar-cell carcinomata.

In one table the authors compare the features of bronchogenic and bronchiolar carcinoma and in another set out the findings in their own 16 cases. Reproductions of radiographs of the chest in 6 of these cases show the variations in type. *A. M. Rackow*

740. **Roentgen Diagnosis of Pericardial Effusion; New Angiocardiographic Observations**
I. STEINBERG, H. V. VON GAL, and N. FINBY. *American Journal of Roentgenology, Radium Therapy, and Nuclear Medicine* [*Amer. J. Roentgenol.*] **79**, 321–332, Feb., 1958. 6 figs., 18 refs.

Angiocardiography was done [at New York Hospital–Cornell Medical Center] in 30 patients with pericardial effusion to differentiate them from large dilated hearts and mediastinal tumors. In every instance, the characteristic feature of pericardial effusion, a heart surrounded by fluid, was demonstrated in frontal view. In the lateral projection, however, the pericardial fluid was always anterior, retrosternal, and infracardiac causing backward displacement of the heart.

It seems that small amounts of pericardial fluid first accumulate below the heart. The fluid extends anteriorly and then appears along the lateral borders of the heart with consequent " straightening ". When massive pericardial effusions occur, the lateral pericardial recesses behave very much like water wings and present laterally. These lateral pouches may fill asymmetrically simulating pericardial or mediastinal masses. It is recommended, in order to avoid traversing the lung, that the anterior or infracardiac approach be used for pericardial paracentesis.

Angiocardiography is recommended for diagnosis of pericardial effusions in problem cases. This method is preferred to diagnostic pericardial paracentesis because enlarged and dilated hearts are easily lacerated. The increasing use of surgery for treatment and biopsy of the pericardium in pericardial effusions also makes preoperative diagnosis imperative.—[Authors' summary.]

741. **Use of Air as a Contrast Medium in the Diagnosis of Intestinal Obstruction of the Newborn**
J. W. HOPE and A. E. O'HARA. *Radiology* [*Radiology*] **70**, 349–361, March, 1958. 9 figs., 10 refs.

An obstructive condition of the bowel in the newborn infant can best be diagnosed by radiological examination, but the authors of this paper from the Children's Hospital of Philadelphia express concern at the amount of radiation these infants may receive in the more usual methods of fluoroscopic examination accompanied by the taking of radiographs. To reduce this radiation risk they advocate that screening should be dispensed with and no opaque contrast medium should be used. In their view air will give all the information needed for a diagnosis, and three, or at the most five, plain radiographs with the infant in different positions should, in the majority of cases, determine the site of obstruction. When the infant's stomach contains little air, fluid may be aspirated from it and replaced with air injected through the stomach tube. Radiographs may then be taken in the supine, erect, lateral decubitus, and inverted postures.

The authors discuss the radiographs, which are reproduced, in 5 cases of duodenal atresia from various causes, 2 cases of small-intestine obstruction, and one case of meconium ileus, in all of which the condition was readily diagnosed in radiographs taken with air as the contrast medium. *A. M. Rackow*

742. **Study of Colon by Use of High-kilovoltage Spot-compression Technique**
S. J. FIGIEL, L. S. FIGIEL, and D. K. RUSH. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **166**, 1269–1275, March 15, 1958. 3 figs., 16 refs.

The authors consider that the present concept that polypoid lesions of the colon are potentially malignant urgently calls for the introduction of a simple, accurate, routine method for their detection since until recently these growths could be detected only by highly specialized studies carried out on carefully selected patients. After evaluating all known techniques they have come to the conclusion that the simplest and most accurate method available combines the use of large-field radiography at high kilovoltage with spot compression of the colon, complemented by routine high-kilovoltage barium-enema films. Preparation of the patient, which they consider to be most important, consists in administration of a liquid non-residue diet during the 24 hours before the examination, a dose of castor oil (30 to 60 ml.) at 6 p.m. on the day before, and cleansing enemas on the evening before and morning of the examination.

Preliminary trials showed that the most satisfactory mixture was 16 oz. (450 g.) of ordinary barium in 3 qt. (2·8 litres) of water, more complex micronized types of barium not being considered necessary. For applying pressure a cone 6·5 in. (16·5 cm.) in diameter and 2·5 in. (6 cm.) in depth was used mounted on a sturdy fluoroscopic screen. All flexures and abnormally appearing segments were exposed during fluoroscopy. After fluoroscopy 120-kV. films in the antero-posterior and both oblique positions were taken, as well as a post-evacuation film, additional filtration of 4 mm. Al being used on the tube. A Lysholm microline stationary grid was preferred to a Bucky grid. Radiation exposure of the radiologist was within accepted limits, and in regard to the patient experiments on a phantom showed that during fluoroscopy the skin of the back did not receive more than 1 r., and 1 r. for each localized exposure, while the anterior abdominal wall received 2·5 r. for each of the three film exposures. These doses were

reduced by 50% at a depth of 5 cm. and, it is pointed out, are considerably below those received when the double-contrast technique is used.

By the method described the detection of very small polyps ranging from 2 to 7 mm. in size was no longer an occasional finding, nor was the detection of multiple lesions uncommon. Arminski and McClean (*Grace Hosp. Bull. (Detroit)*, 1955, **33**, 57) showed that the incidence of malignancy in polyps 5 mm. or less in diameter was less than 0·2%, and in polyps less than 1 cm. in size was less than 2%. Necropsy studies have shown that in patients over 60 years of age the incidence of polyps is as high as 50%. It is suggested that surgery is not necessarily indicated in the older asymptomatic patient with polyps 5 to 7 mm. in size. They should, however, be kept under observation and examined radiologically every 6 months to detect any alteration in size of the growths. *John H. L. Conway-Hughes*

743. **Radiological Changes in Reiter's Syndrome and Arthritis Associated with Urethritis**

R. S. MURRAY, J. K. OATES, and A. C. YOUNG. *Journal of the Faculty of Radiologists* [*J. Fac. Radiol. (Lond.)*] **9**, 37–43, Jan., 1958. 13 figs., 16 refs.

In this article from the London Hospital the authors report a study of 53 patients suffering from Reiter's syndrome. All had arthritis associated with urethritis, but the conjunctivitis which constitutes the third feature of the syndrome tended to be mild and short-lived, and in 34 cases was absent. Elimination of concurrent gonococcal infection by antibiotics in 19 patients showed them to be suffering from the classic non-specific urethritis. In each case differentiation from rheumatoid arthritis was made on clinical grounds. In a review of the literature it was noted that the radiological findings had been reported only in isolated instances and this aspect was therefore studied in particular in the present series.

Radiologically, the most commonly affected areas were the feet, the hands, and the sacro-iliac joints. Spinal changes typical of ankylosing spondylitis were found in 6 cases. The knees, though often clinically affected, rarely showed radiological involvement. The time of appearance of radiological changes was variable. In some cases such changes were evident in the first few weeks or months, being preceded only by periarticular thickening around the small joints of the feet and hands, while in others radiological signs did not develop at all in the course of several years. Erosions of the articular surfaces of the affected joints were common and were invariably accompanied by narrowing of the joint space which might progress to disorganization and subluxation. Periosteal new bone formation of various types was a striking feature in many cases, affecting especially the short bones. Flattening of the arches of the feet, with which dislocation of the metatarso-phalangeal joints was usually associated, was seen in several cases. The radiological differentiation of Reiter's syndrome from rheumatoid arthritis may not be radiologically possible, and the authors consider that in atypical cases of the latter condition in males evidence of urogenital infection should be sought. *R. O. Murray*

744. **Radiological Aspects of Reiter's Syndrome ("Venereal" Arthritis)**

D. F. REYNOLDS and G. W. CSONKA. *Journal of the Faculty of Radiologists* [*J. Fac. Radiol. (Lond.)*] **9**, 44–49, Jan., 1958. 12 figs., 7 refs.

Radiographs from 58 male and 2 female patients with Reiter's syndrome out of a total of 185 seen at St. Mary's Hospital, London, were studied in an attempt to assess the radiological features of the condition. The triad of arthritis, urethritis, and conjunctivitis was present in 35 cases, the last feature being absent in 25. The radiological findings were the same in both groups. Clinically, the arthritis was most common in the distal joints of the lower extremity, the knee and ankle being involved in over 70% of the whole series of 185 cases, the hand and wrist in over 55%, and the sacro-iliac joints in 9%. A valuable summary of the differences between Reiter's syndrome and rheumatoid arthritis is given.

Radiologically, in the acute stage the affected joints showed periarticular thickening and localized bony rarefaction. Swelling of tendons, particularly the tendo achillis and the patellar tendon, could be seen and was regarded as a differentiating feature from rheumatoid arthritis. Periosteal new bone formation was demonstrated in 27% of cases around the small bones of the feet. Plantar spur formation on the os calcis was sometimes observed after an initial stage of erosion in association with a plantar fasciitis. However, some of the spurs were similar to those seen frequently in routine radiography, and caution is necessary in ascribing them to the disease process. In the chronic stage extensive new bone formation often occurred on the plantar aspect of the os calcis, frequently bilaterally, and foot deformities developed subsequently in some cases. If arthritis was persistent the joint space might become narrowed, serial films showing the development of marginal erosions. In the course of healing such erosions were likely to develop a sclerosed edge, but permanent defects were left. The sacro-iliac joints of 34 patients were investigated; pitting of the articular surfaces and subarticular sclerosis were observed in 11, but complete ankylosis was not seen. In only one of these cases were spinal changes observed. Other changes included true bony ankylosis, mainly in the small joints of the feet, in 8 cases, and the Pellegrini–Stieda type of calcification in the knee in 2.

The authors consider that this syndrome is not rare and should be considered in the differential diagnosis of polyarthritis in the male. *R. O. Murray*

745. **Selective Angiography in Renal Tuberculosis.** [In English]

J. FRIMANN-DAHL. *Acta radiologica* [*Acta radiol. (Stockh.)*] **49**, 31–41, Jan. [received March], 1958. 9 figs., 7 refs.

The author describes his experiences of the selective injection of contrast media into the renal artery, a method he has used in the examination of tuberculous kidneys in 23 patients at the Ullevål Hospital, Oslo. An opaque catheter, size 205, is used, the end of which is curved into a slight hook by dipping it into hot water and moulding it. It is fitted with a metal leader and introduced into

the aorta by femoral puncture. The leader keeps the catheter tip straight, but it bends again when the leader is withdrawn. About 8 ml. of 35% " hypaque " (sodium diatrizoate) is injected by hand and serial angiograms are taken.

One important advantage of the selective technique is that the mesenteric vessels do not confuse the field examined. On the other hand aberrant vessels do not fill, and there will be an apparent defect in the parenchyma. In small renal tuberculous foci the vascular changes may consist in slight irregularities of one or more branches of the arteries, or these may be displaced, bent, blocked, or narrowed. In the case of larger lesions several branches may be blocked, producing a poorly vascularized zone, or the arteries may run claw-like round a cavity. *D. E. Fletcher*

746. **Complications of Aortography. Factors Influencing Renal Function following Aortography with 70 per cent. Urokon**

A. C. BEALL, E. S. CRAWFORD, C. M. COUVES, M. E. DEBAKEY, and J. H. MOYER. *Surgery* [*Surgery*] **43**, 364–380, March, 1958. 11 refs.

The renal complications of abdominal aortography have been studied at the Baylor University College of Medicine, Houston, Texas, in experiments performed on 5[illegible] dogs and in the results of renal function tests carried out on 19 patients undergoing percutaneous lumbar aortography. The contrast medium was 70% " urokon sodium " (sodium acetrizoate). The injection caused immediate constriction of the renal arteries, with reduction in the renal blood flow and depression of the glomerular filtration rate. Renal function usually returned to normal after several days, but could be permanently affected if large doses of the contrast medium reached the renal parenchyma.

It is concluded that up to 30 ml. of this contrast medium will not cause renal damage in man unless it is injected directly into a renal artery. Occlusion of the aorta below the renal arteries does not appreciably increase the risk of this complication. *D. E. Fletcher*

747. **The Cholecystogram and the Clinician**

J. D. ROSE. *British Medical Journal* [*Brit. med. J.*] **1**, 360–362, Feb. 15, 1958. 5 figs., 7 refs.

The limitations of cholecystography as normally carried out—" classic cholecystography "—lie in its failure to reveal abnormalities of motor function. The author considers that a high proportion of patients who show clinical evidence of biliary dysfunction and whose cholecystograms appear normal belong to this category.

A technique for serial radiography is described in which, after the usual opacification of the gall-bladder by " telepaque " (iopanoic acid), films are taken in the postero-anterior and lateral positions. Thereafter a fatty meal is given, and serial films are taken at 10-minute intervals for 80 minutes. Measurements are then made of gall-bladder volume, and these are plotted, together with the angle formed between the long axis of the gall-bladder and that of the vertebral column—the " angle of erection ". This normally increases by an amount that varies from 5 to 15 degrees. In cases where there is resistance to emptying by spasm or other obstructive factor the increase of angle is greater; in cases of lax or atonic sphincter the change is less or absent.

Of 137 patients examined by this method, 40 had a normal, classic cholecystogram, but serial radiography revealed dyskinesia which was subsequently confirmed at operation. The most common finding (34 cases) was poor evacuation, in 20 cases shown to be due to muscular atony of the gall-bladder. The other 14 cases were obstructive in nature, 7 being due to spasm of the sphincter of Lütkens and the remainder to valvular obstruction, fibrosis of the cystic duct, or an infundibulocolonic kink.

In 6 cases there was too rapid evacuation of the gall-bladder (hyperkinesia), due either to its irritability in association with duodenal ulcer or chronic cholecystitis or to laxity of the sphincter of Oddi. Four case reports are presented. The author has been led to abandon the orthodox cholecystogram as a result of this experience, and considers that the normal " classic " cholecystogram is misleading in 95% of cases of clinical biliary disease. *A. M. Rackow*

RADIOTHERAPY

748. **Combined Roentgen Therapy and Nitrogen Mustard in Carcinoma of the Lung as Compared to Other Methods**

K. L. KRABBENHOFT and T. LEUCUTIA. *American Journal of Roentgenology, Radium Therapy, and Nuclear Medicine* [*Amer. J. Roentgenol.*] **79**, 491–504, March, 1958. 6 figs., 7 refs.

The authors have reviewed 393 histologically proved cases of bronchial carcinoma out of 788 seen at Harper Hospital, Detroit, between 1922 and 1956, of which 259 (66%) were cases of oat-cell or undifferentiated-cell carcinoma, 82 (20·8%) of squamous-cell, and 35 (8·9%) of adenocarcinoma. Since 1947 nitrogen mustard has been given in combination with *x*-ray therapy and the purpose of this study was to compare the results of such combined therapy with those formerly obtained by other methods; 35 cases which were treated in addition with intrabronchial radium or with nitrogen mustard alone are excluded from the final analysis.

In the 132 cases treated by *x* rays alone and 226 by a combination of *x* rays and nitrogen mustard the average survival times were 8·8 and 7·45 months respectively. However, the authors point out that these figures are somewhat misleading, since the group treated by *x* rays alone contained a limited number of early cases treated with supervoltage radiation among which the survival time was unusually long. These results were reversed when the two methods were compared by the number of patients living less than 3 months, less than 12 months, and over 12 months. In the group treated by radiotherapy alone the percentage survivals for these periods were 37·9, 50, and 12·1 respectively, whereas in the combined-treatment group the corresponding percentages were 29·2, 58·4, and 12·4. The *x*-ray technique for

200 kV. and 550 kV. was by parallel opposing fields over the affected lung and mediastinum, the fields being kept as small as possible in order to protect the lung parenchyma. Very few complications such as lung fibrosis, fistula, or haemorrhage were encountered. [No mention is made of the dose or time or of the technique used in the cases treated by supervoltage radiation.]

The nitrogen mustard was given intravenously in doses of 0·1 mg. per kg. body weight daily for the first 4 consecutive days of *x*-ray therapy, and thereafter the latter was continued alone. Comparison of the results for the various histological types of tumour showed that oat-cell carcinomata received the best palliation from the combined method of therapy. The authors conclude that these results merit the continuation of the treatment of inoperable carcinoma of the lung by a combination of *x*-ray therapy and nitrogen mustard. *K. S. Holmes*

749. **Experiences in the Treatment of Inoperable Carcinoma of the Lung with 2 MV. and Cobalt 60 Irradiation**
R. J. GUTTMANN. *American Journal of Roentgenology, Radium Therapy, and Nuclear Medicine* [*Amer. J. Roentgenol.*] **79**, 505–510, March, 1958. 11 figs., 4 refs.

The author reviews the results in 144 patients with inoperable carcinoma of the lung treated by her at the Francis Delafield Hospital, New York, between January, 1951, and October, 1956, with supervoltage irradiation (the first 100 were reported over 2 years ago (*Cancer*, 1955, **8**, 1254)). Of these cases, all of which were advanced, metastatic, and inoperable, 134 were treated with 2-million-volt *x* rays and 10 with radioactive cobalt (^{60}Co). The author prefers stationary fields to rotation therapy since by the former method less of the healthy neighbouring tissue is exposed to radiation. Treatment was given to two large parallel opposing fields about 15×15 cm. in area. The daily tumour dose was 200 r. and the total tumour dose 5,000 to 6,000 over 5 to 6 weeks. Thus a homogeneous dose was given through the treated areas, while nearby structures such as the spinal cord were spared. Both skin tolerance and general tolerance were excellent. All the tumours were histologically confirmed and were classified as follows: carcinoma (unspecified) 58 cases, squamous-cell carcinoma 44, undifferentiated-cell carcinoma 20, adenocarcinoma 13, oat-cell carcinoma 5, thymoma 2, and mesothelioma 2.

A very high percentage [figure not stated] benefited greatly from the treatment and showed excellent symptomatic improvement, cough, dyspnoea, pain, and haemoptysis tending to disappear. However, most patients showed little or no change radiographically, and in only a minority was there complete disappearance of the lesion after therapy. Thus, the author points out, lack of radiographic change is not necessarily a poor prognostic sign and radiation fibrosis may mask the disappearance of the tumour. Survival times were similar to those in the previous series; thus 96 patients died between 1 and 12 months following treatment, 24 lived more than 18 months (of whom 7 are still living), 18 more than 21 months, 14 more than 2 years, 4 over 4 years (with 2 still alive), and one is still living after 5 years. Necropsy was carried out on 19 patients and showed active disease in the lung, with radiation changes and widespread metastases, in 16, but no sign of active neoplasm in the remaining 3.

The author concludes that malignant lesions of epithelium respond better than those of glandular tissue, and that there is microscopical proof that it is possible to sterilize even a large carcinoma of the lung by means of external radiation. *K. S. Holmes*

750. **Some Observations on the Effect of Cobalt 60 Beam Therapy on Epidermoid Carcinoma during the First Five-year Study Period**
I. H. SMITH and J. S. LOTT. *American Journal of Roentgenology, Radium Therapy, and Nuclear Medicine* [*Amer. J. Roentgenol.*] **79**, 406–414, March, 1958. 6 figs., 4 refs.

Further to a previous survey by Smith (*Canad. med. Ass. J.*, 1957, **77**, 289; *Abstr. Wld Med.*, 1958, **23**, 232) the authors now present their experience of radioactive cobalt (^{60}Co) beam therapy during the first 5-year period at the Cancer Foundation Clinic, London, Ontario, with particular reference to the treatment of epidermoid carcinoma of the oral cavity, larynx, oesophagus, and bladder. Apart from a few cases of oesophageal carcinoma receiving rotational therapy, all cases were treated by fixed-beam therapy, the treatment distance being 80 cm. A description is given of the treatment technique for each tumour site, and optimum dosage is also discussed.

In none of 43 cases of oral cancer which showed no radiological or clinical evidence of bone invasion before treatment did any bone necrosis occur, while of 4 with evidence of invasion of the mandible, none developed bone symptoms after treatment. In 9 cases " clinically positive " solitary lymph nodes were included in the treated volume, and of these patients 7 are alive and well. Of 13 cases of intrinsic cancer of the larynx treated, only 2 developed necrosis of cartilage; in one of these 2 treatment was through large fields (10×17 cm.) because of extensive subglottic spread, and the other patient had previously received irradiation to the larynx as a child. Subglottic extension was present in 6 cases in this group and the disease was successfully controlled in 5 of them. Radical treatment was given in 18 cases of oesophageal cancer.

The complications of treatment, for example, mediastinal fistula, pulmonary fibrosis, and oesophageal stricture, are discussed. The authors do not consider that complications occurred with sufficient frequency to necessitate any alteration in their methods of treatment. Of these patients, 5 survived for periods ranging from 28 to 48 months. Lastly, 22 cases of bladder cancer were treated radically. Considering that in two-thirds of these residual or recurrent disease was present before treatment, the fact that 11 of them were without disease for periods of from 30 to 62 months is considered encouraging. It was noted that no late fibrosis developed in these surviving patients. The advantages of ^{60}Co beam therapy over conventional radiotherapy are briefly summarized. *M. P. Cole*